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=> d his

     (FILE 'HOME' ENTERED AT 12:23:37 ON 28 JUL 2005)

     FILE 'MEDLINE, EMBASE, BIOSIS, BIOTECHDS, SCISEARCH, HCAPLUS, NTIS,
     LIFESCI' ENTERED AT 12:24:27 ON 28 JUL 2005
L1       1340563 S KINASE?
L2        441287 S SERINE OR THREONINE
L3        111458 S L1 AND L2
L4         30908 S "CDC"
L5           285 S L3 AND L4
L6       7187685 S CLON? OR EXPRESS? OR RECOMBINANT
L7           142 S L5 AND L6
L8           112 DUP REM L7 (30 DUPLICATES REMOVED)
L9            63 S HUMAN AND L8
L10          126 S "SERINE AND ARGININE RICH"
L11            1 S L9 AND L10
L12           58 S "CLK4"
L13           48 S L6 AND L12
L14           21 DUP REM L13 (27 DUPLICATES REMOVED)
                 E YAN C/AU
L15         1170 S E3
                 E YE J/AU
L16         1942 S E3
                 E KETCHUM K A/AU
L17          482 S E3-E7
                 E BEASLEY E M/AU
L18          330 S E3
                 E DIFRANCESCO V/AU
L19           97 S E3-E4
L20         3708 S L15 OR L16 OR L17 OR L18 OR L19
L21            0 S L20 AND L5
L22            0 S L12 AND L20
L23            1 S L4 AND L20
L24            0 S L10 AND L20
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=> s kinase?
L1     1340563 KINASE?

=> s serine or threonine
L2      441287 SERINE OR THREONINE

=> s l1 and l2
L3      111458 L1 AND L2

=> s "CDC"
L4       30908 "CDC"

=> s l3 and l4
L5         285 L3 AND L4

=> s clon? or express? or recombinant
   2 FILES SEARCHED...
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   3 FILES SEARCHED...
L6     7187685 CLON? OR EXPRESS? OR RECOMBINANT

=> s l5 and l6
L7          142 L5 AND L6

=> dup rem l7
PROCESSING COMPLETED FOR L7
L8          112 DUP REM L7 (30 DUPLICATES REMOVED)

=> s human and l8
   3 FILES SEARCHED...
L9           63 HUMAN AND L8

=> d 1-63 ibib ab

L9   ANSWER 1 OF 63     MEDLINE on STN
ACCESSION NUMBER:    2005213982     MEDLINE
DOCUMENT NUMBER:     PubMed ID: 15671017
TITLE:               Binding of HTm4 to cyclin-dependent kinase
                     (Cdk)-associated phosphatase (KAP).Cdk2.cyclin A complex
                     enhances the phosphatase activity of KAP, dissociates
                     cyclin A, and facilitates KAP dephosphorylation of Cdk2.
AUTHOR:              Chinami Masanobu; Yano Yoshihiko; Yang Xing; Salahuddin
                     Saira; Moriyama Kosei; Shiroishi Mitsunori; Turner Helen;
                     Shirakawa Taro; Adra Chaker N
CORPORATE SOURCE:    Department of Nutrition, Kyushu Women's University,
                     Jiyugaoka 1-1, Kitakyushushi 807-8586, Japan.
CONTRACT NUMBER:     AI 43663 (NIAID)
SOURCE:              Journal of biological chemistry, (2005 Apr 29) 280 (17)
                     17235-42.  Electronic Publication: 2005-01-24.
                     Journal code: 2985121R. ISSN: 0021-9258.
PUB. COUNTRY:        United States
DOCUMENT TYPE:       Journal; Article; (JOURNAL ARTICLE)
LANGUAGE:            English
FILE SEGMENT:        Priority Journals
ENTRY MONTH:         200506
ENTRY DATE:          Entered STN: 20050426
                     Last Updated on STN: 20050622
                     Entered Medline: 20050621
AB   Cyclin-dependent kinase 2 (cdk2) activation requires
     phosphorylation of Thr160 and dissociation from cyclin A.  The T-loop of
     cdk2 contains a regulatory phosphorylation site at Thr160.  An interaction
     between cdc-associated phosphatase (KAP) and cdk2 compromises
     the interaction between cdk2 and cyclin A, which permits access of KAP, a
     Thr160-directed phosphatase, to its substrate, cdk2.  We have reported
     that KAP is bound and activated by a nuclear membrane protein, HTm4.
     Here, we present in vitro data showing the direct interaction between the
     HTm4 C terminus and KAP Tyr141.  We show that this interaction not only
     facilitates access of KAP to Thr160 and accelerates KAP kinetics, but also
     forces exclusion of cyclin A from the KAP.cdk2 complex.

L9   ANSWER 2 OF 63     MEDLINE on STN
ACCESSION NUMBER:    2005172560     MEDLINE
DOCUMENT NUMBER:     PubMed ID: 15805289
TITLE:               RNA silencing of checkpoint regulators sensitizes
                     p53-defective prostate cancer cells to chemotherapy while
                     sparing normal cells.
AUTHOR:              Mukhopadhyay Utpal K; Senderowicz Adrian M; Ferbeyre
                     Gerardo
CORPORATE SOURCE:    Departement de Biochimie, Universite de Montreal, Montreal,
                     Quebec, Canada.
SOURCE:              Cancer research, (2005 Apr 1) 65 (7) 2872-81.
```

Journal code: 2984705R. ISSN: 0008-5472.
PUB. COUNTRY: United States
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 200505
ENTRY DATE: Entered STN: 20050405
Last Updated on STN: 20050527
Entered Medline: 20050526

AB p53 is frequently mutated in patients with prostate cancer, especially in those with advanced disease. Therefore, the selective elimination of p53 mutant cells will likely have an impact in the treatment of prostate cancer. Because p53 has important roles in cell cycle checkpoints, it has been anticipated that modulation of checkpoint pathways should sensitize p53-defective cells to chemotherapy while sparing normal cells. To test this idea, we knocked down ataxia telangiectasia mutated (ATM) gene by RNA interference in prostate cancer cell lines and in normal **human** diploid fibroblasts IMR90. ATM knockdown in p53-defective PC3 prostate cancer cells accelerated their cell cycle transition, increased both E2F activity and proliferating cell nuclear antigen **expression**, and compromised cell cycle checkpoints, which are normally induced by DNA damage. Consequently, PC3 cells were sensitized to the killing effects of the DNA-damaging drug doxorubicin. Combining ATM knockdown with the Chk1 inhibitor UCN-01 further increased doxorubicin sensitivity in these cells. In contrast, the same strategy did not sensitize either IMR90 or LNCaP prostate cancer cells, both of which have normal p53. However, IMR90 and LNCaP cells became more sensitive to doxorubicin or doxorubicin plus UCN-01 when both p53 and ATM functions were suppressed. In addition, knockdown of the G(2) checkpoint regulators ATR and Chk1 also sensitized PC3 cells to doxorubicin and increased the **expression** of the E2F target gene PCNA. Together, our data support the concept of selective elimination of p53 mutant cells by combining DNA damage with checkpoint inhibitors and suggest a novel mechanistic insight into how such treatment may selectively kill tumor cells.

L9 ANSWER 3 OF 63 MEDLINE on STN
ACCESSION NUMBER: 2004553650 MEDLINE
DOCUMENT NUMBER: PubMed ID: 15525512
TITLE: Phosphorylation of Cdc20 by Bub1 provides a catalytic mechanism for APC/C inhibition by the spindle checkpoint.
AUTHOR: Tang Zhanyun; Shu Hongjun; Oncel Dilhan; Chen She; Yu Hongtao
CORPORATE SOURCE: Department of Pharmacology, The University of Texas Southwestern Medical Center at Dallas, 5323 Harry Hines Boulevard, Dallas, TX 75390, USA.
CONTRACT NUMBER: GM61542 (NIGMS)
SOURCE: Molecular cell, (2004 Nov 5) 16 (3) 387-97.
Journal code: 9802571. ISSN: 1097-2765.
PUB. COUNTRY: United States
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 200412
ENTRY DATE: Entered STN: 20041105
Last Updated on STN: 20041220
Entered Medline: 20041214

AB To ensure the fidelity of chromosome segregation, the spindle checkpoint blocks the ubiquitin ligase activity of APC/C(Cdc20) in response to a single chromatid not properly attached to the mitotic spindle. Here we show that HeLa cells depleted for Bub1 by RNA interference are defective in checkpoint signaling. Bub1 directly phosphorylates Cdc20 in vitro and inhibits the ubiquitin ligase activity of APC/C(Cdc20) catalytically. A Cdc20 mutant with all six Bub1 phosphorylation sites removed is refractory

to Bub1-mediated phosphorylation and inhibition in vitro. Upon checkpoint activation, Bub1 itself is hyperphosphorylated and its **kinase** activity toward Cdc20 is stimulated. Ectopic **expression** of the nonphosphorylatable Cdc20 mutant allows HeLa cells to escape from mitosis in the presence of spindle damage. Therefore, Bub1-mediated phosphorylation of Cdc20 is required for proper checkpoint signaling. We speculate that inhibition of APC/C(Cdc20) by Bub1 in a catalytic fashion may partly account for the exquisite sensitivity of the spindle checkpoint.

L9 ANSWER 4 OF 63 MEDLINE on STN
ACCESSION NUMBER: 2004279248 MEDLINE
DOCUMENT NUMBER: PubMed ID: 15048074
TITLE: The cell cycle checkpoint **kinase** Chk2 is a negative regulator of mitotic catastrophe.
AUTHOR: Castedo Maria; Perfettini Jean-Luc; Roumier Thomas; Yakushijin Kenichi; Horne David; Medema Rene; Kroemer Guido
CORPORATE SOURCE: CNRS-UMR 8125, Institut Gustave Roussy, 39 rue Camille-Desmoulins, F-94805 Villejuif, France.
SOURCE: Oncogene, (2004 May 27) 23 (25) 4353-61. Journal code: 8711562. ISSN: 0950-9232.
PUB. COUNTRY: England: United Kingdom
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 200407
ENTRY DATE: Entered STN: 20040606
Last Updated on STN: 20040702
Entered Medline: 20040701

AB Fusion between nonsynchronized cells leads to the formation of heterokarya which transiently activate Cyclin-dependent **kinase** 1 (Cdk1)/cyclin B1 and enter the prophase of the cell cycle, where they arrest due to a loss of Cdk1/cyclin B1 activity, activate p53, disorganize centrosomes, and undergo apoptosis. Here, we show that the down regulation of Cdk1/cyclin B is secondary to the activation of the DNA structure checkpoint **kinase** Chk2. Thus, syncytia generated by the fusion of asynchronous HeLa cells contain elevated levels of active Chk2 but not Chk1. Chk2 bearing the activating phosphorylation on **threonine**-68 accumulates in BRCA1 nuclear bodies when the cells arrest at the G2/M boundary. Inhibition of Chk2 by transfection of a dominant-negative Chk2 mutant or a chemical inhibitor, debromohymenialdesine, stabilizes centrosomes, maintains high cyclin B1 levels, and allows for a prolonged activation of Cdk1. Under these conditions, multinuclear HeLa syncytia do not arrest at the G2/M boundary and rather enter mitotis and subsequently die during the metaphase of the cell cycle. This mitotic catastrophe is associated with the activation of the pro-apoptotic caspase-3. Inhibition of caspases allows the cells to go beyond the metaphase arrest, indicating that apoptosis is responsible for cell death by mitotic catastrophe. In another, completely different model of mitotic catastrophe, namely 14.3.3 sigma-deficient HCT116 colon carcinoma cells treated with doxorubicin, Chk2 activation was also found to be deficient as compared to 14.3.3 sigma-sufficient controls. Inhibition of Chk2 again facilitated the induction of mitotic catastrophe in HCT116 wild-type cells. In conclusion, a conflict in cell cycle progression or DNA damage can lead to mitotic catastrophe, provided that the checkpoint **kinase** Chk2 is inhibited. Inhibition of Chk2 thus can sensitize proliferating cells to chemotherapy-induced apoptosis.

L9 ANSWER 5 OF 63 MEDLINE on STN
ACCESSION NUMBER: 2004253397 MEDLINE
DOCUMENT NUMBER: PubMed ID: 15064732
TITLE: Cdk2-dependent phosphorylation of the NF-Y transcription factor is essential for the **expression** of the

cell cycle-regulatory genes and cell cycle G1/S and G2/M transitions.

AUTHOR: Chae Hee-Don; Yun Jeanho; Bang Yung-Jue; Shin Deug Y

CORPORATE SOURCE: National Research Laboratory, Department of Microbiology, Dankook University College of Medicine, Cheonan 330-714, Korea.

SOURCE: Oncogene, (2004 May 20) 23 (23) 4084-8.
Journal code: 8711562. ISSN: 0950-9232.

PUB. COUNTRY: England: United Kingdom

DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)

LANGUAGE: English

FILE SEGMENT: Priority Journals

ENTRY MONTH: 200406

ENTRY DATE: Entered STN: 20040521
Last Updated on STN: 20040616
Entered Medline: 20040615

AB We previously reported that cdk2 phosphorylates two **serine** residues near the DNA-binding domain of the YA subunit of NF-Y transcription factor and this phosphorylation is essential for DNA binding of NF-Y. In this study, we examined the effects of a phosphorylation-deficient mutant form of YA, YA-aa, in which the two **serine** residues are replaced with alanine, on the cell cycle and **expression** of the NF-Y target genes. Transient transfection assays show that YA-aa inhibits transcription from the NF-Y target promoters, such as cdc2, cyclin A, and cdc25C. Moreover, this inhibitory function of YA-aa can be suppressed by the **expression** of wild-type YA, implying that YA-aa inhibits transcription of those NF-Y target genes by inactivating wild-type YA. Since NF-Y target genes include the cell cycle-regulatory genes that ensure orderly progression of the cell cycle, we examined the effects of YA-aa in cell cycle progression. We constructed a **recombinant** adenovirus encoding YA-aa and found that YA-aa **expression** leads to repression of cell cycle-regulatory genes, such as cyclin A, RNR R2, DNA polymerase alpha, cdc2, cyclin B, and cdc25C. Consistently, YA-aa **expression** results in the inactivation of both cdc2 and cdk2. Furthermore, cell cycle analysis reveals that YA-aa induces cell cycle arrest at both G1 and G2/M. These results suggest that cdk2-dependent phosphorylation of NF-Y is essential for the **expression** of the cell cycle-regulatory genes and therefore for cell cycle progression at both G1/S and G2/M.

L9 ANSWER 6 OF 63 MEDLINE on STN

ACCESSION NUMBER: 2004251861 MEDLINE

DOCUMENT NUMBER: PubMed ID: 15149599

TITLE: Telomere shortening triggers senescence of **human** cells through a pathway involving ATM, p53, and p21(CIP1), but not p16(INK4a).

COMMENT: Comment in: Mol Cell. 2004 May 21;14(4):420-1. PubMed ID: 15149591

AUTHOR: Herbig Utz; Jobling Wendy A; Chen Benjamin P C; Chen David J; Sedivy John M

CORPORATE SOURCE: Department of Molecular Biology, Cell Biology and Biochemistry, Brown University, Providence, RI 02912, USA.

CONTRACT NUMBER: F32 CA099388 (NCI)
P20 RR-15578 (NCRR)
R01 AG16694 (NIA)
R01 AG18949 (NIA)
R01 CA50519 (NCI)
T32 GM-07601 (NIGMS)

SOURCE: Molecular cell, (2004 May 21) 14 (4) 501-13.
Journal code: 9802571. ISSN: 1097-2765.

PUB. COUNTRY: United States

DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)

LANGUAGE: English

FILE SEGMENT: Priority Journals
ENTRY MONTH: 200407
ENTRY DATE: Entered STN: 20040520
Last Updated on STN: 20040714
Entered Medline: 20040713

AB Cellular senescence can be triggered by telomere shortening as well as a variety of stresses and signaling imbalances. We used multiparameter single-cell detection methods to investigate upstream signaling pathways and ensuing cell cycle checkpoint responses in **human** fibroblasts. Telomeric foci containing multiple DNA damage response factors were assembled in a subset of senescent cells and signaled through ATM to p53, upregulating p21 and causing G1 phase arrest. Inhibition of ATM **expression** or activity resulted in cell cycle reentry, indicating that stable arrest requires continuous signaling. ATR **kinase** appears to play a minor role in normal cells but in the absence of ATM elicited a delayed G2 phase arrest. These pathways do not affect **expression** of p16, which was upregulated in a telomere- and DNA damage-independent manner in a subset of cells. Distinct senescence programs can thus progress in parallel, resulting in mosaic cultures as well as individual cells responding to multiple signals.

L9 ANSWER 7 OF 63 MEDLINE on STN
ACCESSION NUMBER: 2003312788 MEDLINE
DOCUMENT NUMBER: PubMed ID: 12840909
TITLE: Multiple defects of cell cycle checkpoints in U937-ASPI3K, an U937 cell mutant stably **expressing** anti-sense ATM gene cDNA.
AUTHOR: Zhou J; Liu W; Sun L; Sun H; Tang Y
CORPORATE SOURCE: Department of Hematology, Tongji Hospital, Tongji Medical University, Wuhan 430030.
SOURCE: Journal of Tongji Medical University = T'ung chi i k'o ta hsueh hsueh pao, (2000) 20 (4) 273-6.
Journal code: 8605495. ISSN: 0257-716X.
PUB. COUNTRY: China
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 200312
ENTRY DATE: Entered STN: 20030705
Last Updated on STN: 20031218
Entered Medline: 20031217

AB (Ataxia-telangiectasia mutated gene (ATM) functions in control of cell cycle checkpoints in responding to DNA damage and protects cells from undergoing apoptosis. Knock-out within tumor cells of endogenous ATM will achieve therapeutic benefits and enable a better understanding of the decisive mechanisms of cell death or survival in response to DNA damaging agents.) In present paper, we sought to characterize the cell cycle checkpoint profiles in U937-ASPI3K, a U937 cell mutant that was previously established with endogenous ATM knock-out phenotype. Synchronized U937-ASPI3K was exposed to 137Cs irradiation, G1, S, G2/M cell cycle checkpoint profiles were evaluated by determining cell cycle kinetics, p53/p21 protein, cyclin dependent **kinase** 2 (CDK2) and p34CDC2 **kinase** activity in response to irradiation. U937-ASPI3K exhibited multiple defects in cell cycle checkpoints as defined by failing to arrest cells upon irradiation. The accumulation of cellular p53/p21 protein and inhibition of CDK **kinase** was also abolished in U937-ASPI3K. It was concluded that the stable **expression** of anti-sense PI3K cDNA fragment completely abolished multiple cell cycle checkpoints in U937-ASPI3K, and hence U937-ASPI3K with an AT-like phenotype could serves as a valuable model system for investigating the signal transduction pathway in responding to DNA damaging-based cancer therapy.

L9 ANSWER 8 OF 63 MEDLINE on STN

ACCESSION NUMBER: 2003293445 MEDLINE
DOCUMENT NUMBER: PubMed ID: 12820434
TITLE: Phenylacetate inhibits growth and modulates cell cycle gene **expression** in renal cancer cell lines.
AUTHOR: Franco Omar E; Onishi Takehisa; Umeda Yoshiki; Soga Norihito; Wakita Toshiaki; Arima Kiminobu; Yanagawa Makoto; Sugimura Yoshiki
CORPORATE SOURCE: Department of Urology, Mie University School of Medicine, 2-174 Edobashi, Tsu, Mie 514-8507, Japan.
SOURCE: Anticancer research, (2003 Mar-Apr) 23 (2B) 1637-42. Journal code: 8102988. ISSN: 0250-7005.
PUB. COUNTRY: Greece
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 200307
ENTRY DATE: Entered STN: 20030625
Last Updated on STN: 20030726
Entered Medline: 20030725

AB BACKGROUND: Phenylacetate (PA), an aromatic fatty acid, is now undergoing evaluation as a potential anticancer reagent. Our previous study showed that PA induces cell growth inhibition in prostate cancer cells. Here, we investigated whether PA is effective against three renal cancer cell lines in vitro. MATERIALS AND METHODS: The cell viability of PA-treated renal carcinoma cell lines (Caki-1, Os-RC-2 and RCC10) was assessed by trypan-blue exclusion and cell cycle distribution by flow cytometry. The cell cycle-regulatory protein **expression** was evaluated by Western blot, immunoprecipitation and **kinase** assay. RESULTS: Growth inhibition occurred with PA treatment at a dose of 2-5 mM and an increased percentage of cells in G1 after 24 hours of exposure. Reduced phosphorylation of the retinoblastoma protein (Rb) and CDK2 activity, increased **expression** of p21Cip1 and enhanced binding of p21Cip1 to CDK2 were observed following treatment with PA. CONCLUSION: Overall, these results suggest that p21Cip1 is a critical target in PA-mediated cell growth inhibition in RCC cells playing a key role in CDK2 inactivation, hypophosphorylation of pRb and subsequent G1 cell cycle arrest.

L9 ANSWER 9 OF 63 MEDLINE on STN
ACCESSION NUMBER: 2003291743 MEDLINE
DOCUMENT NUMBER: PubMed ID: 12819135
TITLE: Exploration of the cell-cycle genes found within the RIKEN FANTOM2 data set.
AUTHOR: Forrest Alistair R R; Taylor Darrin; Grimmond Sean
CORPORATE SOURCE: The Institute for Molecular Bioscience, University of Queensland, Queensland Q4072, Australia. (RIKEN GER Group; GSL Members). a.forrest@imb.uq.edu.au
SOURCE: Genome research, (2003 Jun) 13 (6B) 1366-75. Journal code: 9518021. ISSN: 1088-9051.
PUB. COUNTRY: United States
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 200308
ENTRY DATE: Entered STN: 20030624
Last Updated on STN: 20030812
Entered Medline: 20030811

AB The cell cycle is one of the most fundamental processes within a cell. Phase-dependent **expression** and cell-cycle checkpoints require a high level of control. A large number of genes with varying functions and modes of action are responsible for this biology. In a targeted exploration of the FANTOM2-Variable Protein Set, a number of mouse homologs to known cell-cycle regulators as well as novel members of

cell-cycle families were identified. Focusing on two prototype cell-cycle families, the cyclins and the NIMA-related **kinases** (NEKs), we believe we have identified all of the mouse members of these families, 24 cyclins and 10 NEKs, and mapped them to ENSEMBL transcripts. To attempt to globally identify all potential cell cycle-related genes within mouse, the MGI (Mouse Genome Database) assignments for the RIKEN Representative Set (RPS) and the results from two homology-based queries were merged. We identified 1415 genes with possible cell-cycle roles, and 1758 potential paralogs. We comment on the genes identified in this screen and evaluate the merits of each approach.

L9 ANSWER 10 OF 63 MEDLINE on STN
ACCESSION NUMBER: 2003290156 MEDLINE
DOCUMENT NUMBER: PubMed ID: 12810625
TITLE: Both DNA topoisomerase II-binding protein 1 and BRCA1 regulate the G2-M cell cycle checkpoint.
AUTHOR: Yamane Kazuhiko; Chen Junjie; Kinsella Timothy J
CORPORATE SOURCE: Department of Radiation Oncology, Case Western Reserve University, Cleveland, Ohio 44106-4942, USA.
CONTRACT NUMBER: CA84578 (NCI)
SOURCE: Cancer research, (2003 Jun 15) 63 (12) 3049-53. Journal code: 2984705R. ISSN: 0008-5472.
PUB. COUNTRY: United States
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 200307
ENTRY DATE: Entered STN: 20030624
Last Updated on STN: 20030729
Entered Medline: 20030728

AB Cell cycle checkpoints play a central role in genomic stability. The **human** DNA topoisomerase II-binding protein 1 (TopBP1) protein contains eight BRCA1 COOH terminus motifs and shares similarities with Cut5, a yeast checkpoint Rad protein. TopBP1 also shares many features with BRCA1. We report that, when **expression** of TopBP1 protein is inhibited in BRCA1 mutant cells, mimicking a TopBP1, BRCA1 double-negative condition, the G(2)-M checkpoint is strongly abrogated and apoptosis is increased after ionizing radiation. However, a BRCA1-negative or a TopBP1-negative background resulted in only partial abrogation of the G(2)-M checkpoint. The BRCA1 mutant and TopBP1-reduced condition specifically destroys regulation of the Chk1 **kinase** but not the Chk2 **kinase**, suggesting involvement in the ataxia telangiectasia-related pathway. These results indicate that both TopBP1 and BRCA1 specifically regulate the G(2)-M checkpoint, partially compensating each function.

L9 ANSWER 11 OF 63 MEDLINE on STN
ACCESSION NUMBER: 2003271993 MEDLINE
DOCUMENT NUMBER: PubMed ID: 12799187
TITLE: Rho protein-mediated changes in the structure of the actin cytoskeleton regulate **human** inducible NO synthase gene **expression**.
AUTHOR: Witteck Andrea; Yao Ying; Fechir Marcel; Forstermann Ulrich; Kleinert Hartmut
CORPORATE SOURCE: Department of Pharmacology, Johannes Gutenberg University, Obere Zahlbacher Strasse 67, D-55101, Mainz, Germany.
SOURCE: Experimental cell research, (2003 Jul 1) 287 (1) 106-15. Journal code: 0373226. ISSN: 0014-4827.
PUB. COUNTRY: United States
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 200307

ENTRY DATE: Entered STN: 20030612
Last Updated on STN: 20030801
Entered Medline: 20030731

AB Rho proteins (Rho, Rac, **Cdc** 42) are known to control the organization of the actin cytoskeleton as well as gene **expression**. Inhibition of Rho proteins by Clostridium difficile toxin B disrupted the F-actin cytoskeleton and enhanced cytokine-induced inducible nitric oxide synthase (iNOS) **expression** in **human** epithelial cells. Also specific inhibition by Y-27632 of p160ROCK, which mediates Rho effects on actin fibers, caused a disruption of the actin cytoskeleton and a superinduction of cytokine-induced iNOS **expression**. Accordingly, direct disruption of the actin cytoskeleton by cytochalasin D, latrunculin B, or jasplakinolide enhanced cytokine-induced iNOS **expression**. The transcription factor serum response factor (SRF) has been described as mediating actin cytoskeleton-dependent regulation of gene **expression**. Direct targets of SRF are activating protein 1 (AP1)-dependent genes. All compounds used inhibited SRF- and AP1-dependent reporter gene **expression** in DLD-1 cells. However, the enhancing effect of the actin cytoskeleton-disrupting compounds on **human** iNOS promoter activity was much less pronounced than the effect on iNOS mRNA **expression**. Therefore, besides transcriptional mechanisms, posttranscriptional effects seem to be involved in the regulation of iNOS **expression** by the above compounds. In conclusion, our data suggest that Rho protein-mediated changes of the actin cytoskeleton negatively modulate the **expression** of **human** iNOS.

L9 ANSWER 12 OF 63 MEDLINE on STN
ACCESSION NUMBER: 2003213098 MEDLINE
DOCUMENT NUMBER: PubMed ID: 12734423
TITLE: Clinical impact of ATR checkpoint signalling failure in **humans**.
AUTHOR: O'Driscoll Mark; Jeggo Penny A
CORPORATE SOURCE: Genome Damage and Stability Centre, University of Sussex, Brighton, East Sussex BN1 9RQ, UK.
SOURCE: Cell cycle (Georgetown, Tex.), (2003 May-Jun) 2 (3) 194-5. Ref: 26
Journal code: 101137841. ISSN: 1538-4101.
PUB. COUNTRY: United States
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
General Review; (REVIEW)
(REVIEW, TUTORIAL)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 200309
ENTRY DATE: Entered STN: 20030508
Last Updated on STN: 20031001
Entered Medline: 20030930

L9 ANSWER 13 OF 63 MEDLINE on STN
ACCESSION NUMBER: 2003198267 MEDLINE
DOCUMENT NUMBER: PubMed ID: 12571229
TITLE: Bikunin target genes in ovarian cancer cells identified by microarray analysis.
AUTHOR: Suzuki Mika; Kobayashi Hiroshi; Tanaka Yoshiko; Hirashima Yasuyuki; Kanayama Naohiro; Takei Yuji; Saga Yasushi; Suzuki Mitsuaki; Itoh Hiroshi; Terao Toshihiko
CORPORATE SOURCE: Department of Obstetrics and Gynecology, Hamamatsu University School of Medicine, Handayama 1-20-1, Hamamatsu, Shizuoka 431-3192, Japan.
SOURCE: Journal of biological chemistry, (2003 Apr 25) 278 (17) 14640-6. Electronic Publication: 2003-02-05.
Journal code: 2985121R. ISSN: 0021-9258.

PUB. COUNTRY: United States
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 200307
ENTRY DATE: Entered STN: 20030430
Last Updated on STN: 20030717
Entered Medline: 20030716

AB Bikunin, a Kunitz-type protease inhibitor, could potentially suppress tumor cell invasion and metastasis. Our previous study revealed that overexpression of bikunin in a **human** ovarian cancer cell line, HRA, resulted in a down-regulation in uPA and uPAR gene **expression**. For identifying the full repertoire of bikunin-regulated genes, a cDNA microarray hybridization screening was conducted using mRNA from bikunin-treated or bikunin-transfected HRA cells. A number of bikunin-regulated genes were identified, and their regulation was confirmed by Northern blot analysis. Our screen identified 11 bikunin-stimulated genes and 29 bikunin-repressed genes. The identified genes can indeed be classified into distinct subsets. These include transcriptional regulators, oncogenes/tumor suppressor genes, signaling molecules, growth/cell cycle, invasion/metastasis, cytokines, apoptosis, ion channels, extracellular matrix proteins, as well as some proteases. This screen identified suppression of several genes such as **CDC**-like **kinase**, LIM domain binding, Ets domain transcription factor, Rho GTPase-activating protein, tyrosine phosphorylation-regulated **kinase**, hyaluronan-binding protein, matriptase, and pregnancy-associated plasma protein-A (PAPP-A), which have previously been implicated in enhancing tumor promotion. Northern blot analysis confirmed that several genes including matriptase and PAPP-A were down-regulated by bikunin by approximately 9-fold. Further, genetic inhibition of matriptase or PAPP-A could lead to diminished invasion. These results show that bikunin alters the pattern of gene **expression** in HRA cells leading to a block in cell invasion.

L9 ANSWER 14 OF 63 MEDLINE on STN
ACCESSION NUMBER: 2003049625 MEDLINE
DOCUMENT NUMBER: PubMed ID: 12559175
TITLE: AURORA-A amplification overrides the mitotic spindle assembly checkpoint, inducing resistance to Taxol.
AUTHOR: Anand Shubha; Penrhyn-Lowe Sue; Venkitaraman Ashok R
CORPORATE SOURCE: CR UK Department of Oncology and The medical Research Council Cancer Cell Unit, Hutchison/MRC Research Centre, University of Cambridge, Hills Road, Cambridge CB2 2XZ, United Kingdom.
SOURCE: Cancer cell, (2003 Jan) 3 (1) 51-62.
Journal code: 101130617. ISSN: 1535-6108.
PUB. COUNTRY: United States
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 200307
ENTRY DATE: Entered STN: 20030202
Last Updated on STN: 20030725
Entered Medline: 20030724

AB The **serine-threonine kinase** gene AURORA-A is commonly amplified in epithelial malignancies. Here we show that elevated Aurora-A **expression** at levels that reflect cancer-associated gene amplification overrides the checkpoint mechanism that monitors mitotic spindle assembly, inducing resistance to the chemotherapeutic agent paclitaxel (Taxol). Cells overexpressing Aurora-A inappropriately enter anaphase despite defective spindle formation, and the persistence of Mad2 at the kinetochores, marking continued activation of the spindle assembly checkpoint. Mitosis is subsequently arrested by failure to

complete cytokinesis, resulting in multinucleation. This abnormality is relieved by an inhibitory mutant of BUB1, linking the mitotic abnormalities provoked by Aurora-A overexpression to spindle checkpoint activity. Consistent with this conclusion, elevated Aurora-A **expression** causes resistance to apoptosis induced by Taxol in a **human** cancer cell line.

L9 ANSWER 15 OF 63 MEDLINE on STN
ACCESSION NUMBER: 2002704533 MEDLINE
DOCUMENT NUMBER: PubMed ID: 12446774
TITLE: An ATR- and Chk1-dependent S checkpoint inhibits replicon initiation following UVC-induced DNA damage.
AUTHOR: Heffernan Timothy P; Simpson Dennis A; Frank Alexandra R; Heinloth Alexandra N; Paules Richard S; Cordeiro-Stone Marila; Kaufmann William K
CORPORATE SOURCE: Department of Pathology and Laboratory Medicine, Center for Environmental Health and Susceptibility, and Lineberger Comprehensive Cancer Center, University of North Carolina, Chapel Hill, North Carolina 27599, USA.
CONTRACT NUMBER: CA55065 (NCI)
CA81343 (NCI)
P30-CA16086 (NCI)
P30-ES10126 (NIEHS)
SOURCE: Molecular and cellular biology, (2002 Dec) 22 (24) 8552-61. Journal code: 8109087. ISSN: 0270-7306.
PUB. COUNTRY: United States
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 200301
ENTRY DATE: Entered STN: 20021217
Last Updated on STN: 20030218
Entered Medline: 20030113
AB Inhibition of replicon initiation is a stereotypic DNA damage response mediated through S checkpoint mechanisms not yet fully understood. Studies were undertaken to elucidate the function of checkpoint proteins in the inhibition of replicon initiation following irradiation with 254 nm UV light (UVC) of diploid **human** fibroblasts immortalized by the ectopic **expression** of telomerase. Velocity sedimentation analysis of nascent DNA molecules revealed a 50% inhibition of replicon initiation when normal **human** fibroblasts were treated with a low dose of UVC (1 J/m(2)). Ataxia telangiectasia (AT), Nijmegen breakage syndrome (NBS), and AT-like disorder fibroblasts, which lack an S checkpoint response when exposed to ionizing radiation, responded normally when exposed to UVC and inhibited replicon initiation. Pretreatment of normal and AT fibroblasts with caffeine or UCN-01, inhibitors of ATR (AT mutated and Rad3 related) and Chk1, respectively, abolished the S checkpoint response to UVC. Moreover, overexpression of **kinase** -inactive ATR in U2OS cells severely attenuated UVC-induced Chk1 phosphorylation and reversed the UVC-induced inhibition of replicon initiation, as did overexpression of **kinase**-inactive Chk1. Taken together, these data suggest that the UVC-induced S checkpoint response of inhibition of replicon initiation is mediated by ATR signaling through Chk-1 and is independent of ATM, Nbs1, and Mre11.

L9 ANSWER 16 OF 63 MEDLINE on STN
ACCESSION NUMBER: 2002643510 MEDLINE
DOCUMENT NUMBER: PubMed ID: 12391152
TITLE: Activation of Akt/protein **kinase** B overcomes a G(2)/m cell cycle checkpoint induced by DNA damage.
AUTHOR: Kandel Eugene S; Skeen Jennifer; Majewski Nathan; Di Cristofano Antonio; Pandolfi Pier Paolo; Feliciano Claudine S; Gartel Andrei; Hay Nissim

CORPORATE SOURCE: Department of Molecular Genetics, College of Medicine, University of Illinois at Chicago, Chicago, Illinois 60607, USA.
CONTRACT NUMBER: AG16927 (NIA)
CA90764 (NCI)
SOURCE: Molecular and cellular biology, (2002 Nov) 22 (22) 7831-41. Journal code: 8109087. ISSN: 0270-7306.
PUB. COUNTRY: United States
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 200212
ENTRY DATE: Entered STN: 20021030
Last Updated on STN: 20021217
Entered Medline: 20021203

AB Activation of Akt, or protein **kinase** B, is frequently observed in **human** cancers. Here we report that Akt activation via overexpression of a constitutively active form or via the loss of PTEN can overcome a G(2)/M cell cycle checkpoint that is induced by DNA damage. Activated Akt also alleviates the reduction in CDC2 activity and mitotic index upon exposure to DNA damage. In addition, we found that PTEN null embryonic stem (ES) cells transit faster from the G(2)/M to the G(1) phase of the cell cycle when compared to wild-type ES cells and that inhibition of phosphoinositol-3-**kinase** (PI3K) in HEK293 cells elicits G(2) arrest that is alleviated by activated Akt. Furthermore, the transition from the G(2)/M to the G(1) phase of the cell cycle in Akt1 null mouse embryo fibroblasts (MEFs) is attenuated when compared to that of wild-type MEFs. These results indicate that the PI3K/PTEN/Akt pathway plays a role in the regulation of G(2)/M transition. Thus, cells **expressing** activated Akt continue to divide, without being eliminated by apoptosis, in the presence of continuous exposure to mutagen and accumulate mutations, as measured by inactivation of an exogenously **expressed** herpes simplex virus thymidine **kinase** (HSV-tk) gene. This phenotype is independent of p53 status and cannot be reproduced by overexpression of Bcl-2 or Myc and Bcl-2 but seems to counteract a cell cycle checkpoint mediated by DNA mismatch repair (MMR). Accordingly, restoration of the G(2)/M cell cycle checkpoint and apoptosis in MMR-deficient cells, through reintroduction of the missing component of MMR, is alleviated by activated Akt. We suggest that this new activity of Akt in conjunction with its antiapoptotic activity may contribute to genetic instability and could explain its frequent activation in **human** cancers.

L9 ANSWER 17 OF 63 MEDLINE on STN
ACCESSION NUMBER: 2002444010 MEDLINE
DOCUMENT NUMBER: PubMed ID: 12202036
TITLE: salvador Promotes both cell cycle exit and apoptosis in Drosophila and is mutated in **human** cancer cell lines.
COMMENT: Comment in: Cell. 2002 Aug 23;110(4):403-6. PubMed ID: 12202030
AUTHOR: Tapon Nicolas; Harvey Kieran F; Bell Daphne W; Wahrer Doke C R; Schiripo Taryn A; Haber Daniel A; Hariharan Iswar K
CORPORATE SOURCE: Massachusetts General Hospital Cancer Center, Building 149, 13th Street, Charlestown 02129, USA.
CONTRACT NUMBER: CA87691 (NCI)
EY11632 (NEI)
GM61672 (NIGMS)
SOURCE: Cell, (2002 Aug 23) 110 (4) 467-78. Journal code: 0413066. ISSN: 0092-8674.
PUB. COUNTRY: United States
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English

FILE SEGMENT: Priority Journals
ENTRY MONTH: 200209
ENTRY DATE: Entered STN: 20020831
Last Updated on STN: 20020925
Entered Medline: 20020924

AB The number of cells in an organism is determined by regulating both cell proliferation and cell death. Relatively few mechanisms have been identified that can modulate both of these processes. In a screen for Drosophila mutations that result in tissue overgrowth, we identified salvador (sav), a gene that promotes both cell cycle exit and cell death. Elevated Cyclin E and DIAP1 levels are found in mutant cells, resulting in delayed cell cycle exit and impaired apoptosis. Salvador contains two WW domains and binds to the Warts (or LATS) protein **kinase**. The **human** ortholog of salvador (hWW45) is mutated in three cancer cell lines. Thus, salvador restricts cell numbers in vivo by functioning as a dual regulator of cell proliferation and apoptosis.

L9 ANSWER 18 OF 63 MEDLINE on STN
ACCESSION NUMBER: 2002365885 MEDLINE
DOCUMENT NUMBER: PubMed ID: 12094328
TITLE: A CHEK2 genetic variant contributing to a substantial fraction of familial breast cancer.
AUTHOR: Vahteristo Pia; Bartkova Jirina; Eerola Hannaleena; Syrjakoski Kirsi; Ojala Salla; Kilpivaara Outi; Tamminen Anitta; Kononen Juha; Aittomaki Kristiina; Heikkila Paivi; Holli Kaija; Blomqvist Carl; Bartek Jiri; Kallioniemi Olli-P; Nevanlinna Heli
CORPORATE SOURCE: Department of Obstetrics and Gynecology, Helsinki University Central Hospital, Haartmaninkatu 8, FIN-00029 HUS, Helsinki, Finland.
SOURCE: American journal of human genetics, (2002 Aug) 71 (2) 432-8. Electronic Publication: 2002-07-28.
Journal code: 0370475. ISSN: 0002-9297.
PUB. COUNTRY: United States
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
OTHER SOURCE: OMIM-MIM113705; OMIM-MIM151623; OMIM-MIM600185; OMIM-MIM604373
ENTRY MONTH: 200208
ENTRY DATE: Entered STN: 20020712
Last Updated on STN: 20030105
Entered Medline: 20020820

AB CHEK2 (previously known as "CHK2") is a cell-cycle-checkpoint **kinase** that phosphorylates p53 and BRCA1 in response to DNA damage. A protein-truncating mutation, 1100delC in exon 10, which abolishes the **kinase** function of CHEK2, has been found in families with Li-Fraumeni syndrome (LFS) and in those with a cancer phenotype that is suggestive of LFS, including breast cancer. In the present study, we found that the frequency of 1100delC was 2.0% among an unselected population-based cohort of 1,035 patients with breast cancer. This was slightly, but not significantly (P=.182), higher than the 1.4% frequency found among 1,885 population control subjects. However, a significantly elevated frequency was found among those 358 patients with a positive family history (11/358 [3.1%]; odds ratio [OR] 2.27; 95% confidence interval [CI] 1.11-4.63; P=.021, compared with population controls). Furthermore, patients with bilateral breast cancer were sixfold more likely to be 1100delC carriers than were patients with unilateral cancer (95% CI 1.87-20.32; P=.007). Analysis of the 1100delC variant in an independent set of 507 patients with familial breast cancer with no BRCA1 and BRCA2 mutations confirmed a significantly elevated frequency of 1100delC (28/507 [5.5%]; OR 4.2; 95% CI 2.4-7.2; P=.0002), compared with controls, with a high frequency also seen in patients with

only a single affected first-degree relative (18/291 [6.2%]). Finally, tissue microarray analysis indicated that breast tumors from patients with 1100delC mutations show reduced CHEK2 immunostaining. The results suggest that CHEK2 acts as a low-penetrance tumor-suppressor gene in breast cancer and that it makes a significant contribution to familial clustering of breast cancer-including families with only two affected relatives, which are more common than families that include larger numbers of affected women.

L9 ANSWER 19 OF 63 MEDLINE on STN
ACCESSION NUMBER: 2002339099 MEDLINE
DOCUMENT NUMBER: PubMed ID: 12082606
TITLE: Nbs1 promotes ATM dependent phosphorylation events including those required for G1/S arrest.
AUTHOR: Girard Pierre-Marie; Riballo Enriqueta; Begg Adrian C; Waugh Alastair; Jeggo Penny A
CORPORATE SOURCE: MRC Cell Mutation Unit, University of Sussex, Brighton, East Sussex, BN1 9RR, UK.
SOURCE: Oncogene, (2002 Jun 20) 21 (27) 4191-9. Journal code: 8711562. ISSN: 0950-9232.
PUB. COUNTRY: England: United Kingdom
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 200207
ENTRY DATE: Entered STN: 20020626
Last Updated on STN: 20020724
Entered Medline: 20020723

AB Cell lines from Nijmegen Breakage Syndrome (NBS) and ataxia telangiectasia (A-T) patients show defective S phase checkpoint arrest. In contrast, only A-T but not NBS cells are significantly defective in radiation-induced G1/S arrest. Phosphorylation of some ATM substrates has been shown to occur in NBS cells. It has, therefore, been concluded that Nbs1 checkpoint function is S phase specific. Here, we have compared NBS with A-T cell lines (AT-5762ins137) that **express** a low level of normal ATM protein to evaluate the impact of residual Nbs1 function in NBS cells. The radiation-induced cell cycle response of these NBS and 'leaky' A-T cells is almost identical; normal G2/M arrest after 2 Gy, intermediate G1/S arrest depending on the dose and an A-T-like S phase checkpoint defect. Thus, the checkpoint assays differ in their sensitivity to low ATM activity. Radiation-induced phosphorylation of the ATM-dependent substrates Chk2, RPAp34 and p53-Ser15 are similarly impaired in AT-5762ins137 and NBS cells in a dose dependent manner. In contrast, NBS cells show normal ability to activate ATM **kinase** following irradiation in vitro and in vivo. We propose that Nbs1 facilitates ATM-dependent phosphorylation of multiple downstream substrates, including those required for G1/S arrest.

L9 ANSWER 20 OF 63 MEDLINE on STN
ACCESSION NUMBER: 2002099662 MEDLINE
DOCUMENT NUMBER: PubMed ID: 11830524
TITLE: Identification of molecular targets associated with selenium-induced growth inhibition in **human** breast cells using cDNA microarrays.
AUTHOR: Dong Yan; Ganther Howard E; Stewart Carleton; Ip Clement
CORPORATE SOURCE: Department of Experimental Pathology, Roswell Park Cancer Institute, Elm and Carlton Streets, Buffalo, NY 14263, USA.
CONTRACT NUMBER: CA 16056 (NCI)
CA 27706 (NCI)
CA 45164 (NCI)
SOURCE: Cancer research, (2002 Feb 1) 62 (3) 708-14. Journal code: 2984705R. ISSN: 0008-5472.
PUB. COUNTRY: United States

DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 200203
ENTRY DATE: Entered STN: 20020207
Last Updated on STN: 20020307
Entered Medline: 20020305

AB Past research indicated that methylseleninic acid (MSA) is an excellent tool for investigating the cancer chemopreventive action of selenium in vitro. The present study was designed to examine the cellular and molecular effects of MSA in the MCF10AT1 and MCF10AT3B premalignant **human** breast cells. After exposure to MSA, both cell lines exhibited a dose- and time-dependent growth-inhibitory response as determined by the 3-(4,5-dimethylthiazol-2-yl)-2,5-diphenyltetrazolium bromide (MTT) cell proliferation assay. Further characterization of cellular and molecular changes was carried out only with the MCF10AT1 cells. Flow cytometry analysis showed that MSA blocked cell cycle progression at the G(0)-G(1) phase. Induction of apoptosis was also observed with the use of either the terminal deoxynucleotidyl transferase-mediated dUTP nick end labeling (TUNEL) or the annexin V binding method. cDNA microarray analyses with cell cycle- and apoptosis-targeted arrays were then applied to profile the gene **expression** changes mediating these two cellular events. The analyses were conducted at 6 and 12 h of MSA treatment using synchronized cells. The **expression** signals of 30 genes were found to be significantly altered by MSA. These genes fall into three categories: cell cycle checkpoint controllers (e.g., cyclins, **cdcs**, cdks, E2F family proteins, and **serine/threonine kinases**), apoptosis regulatory genes (e.g., Apo-3, c-jun, and cdk5/cyclin D1), and signaling molecules [e.g., mitogen-activated protein (MAP)/extracellular signal-regulated protein **kinase** (ERK) and phosphatidylinositol 3'-**kinase** (PI3k) cascade genes]. The **expression** changes of 15 genes were selected for verification by Western or semiquantitative reverse transcription-PCR analyses. An agreement rate of 60% (9 of 15) was obtained from these confirmation experiments. On the basis of the above findings, tentative signaling pathways mediating the outcome of selenium-induced cell cycle arrest and apoptosis are proposed. The present study thus demonstrated the feasibility of applying cDNA microarray technology in delineating the mechanisms of the action of selenium and in pinpointing molecular targets as potential biomarkers for evaluating the efficacy of selenium intervention.

L9 ANSWER 21 OF 63 MEDLINE on STN
ACCESSION NUMBER: 2001653679 MEDLINE
DOCUMENT NUMBER: PubMed ID: 11704824
TITLE: Protein **kinase** CK2 is involved in G2 arrest and apoptosis following spindle damage in epithelial cells.
COMMENT: Erratum in: Oncogene 2002 Apr;21(15):2446
AUTHOR: Sayed M; Pelech S; Wong C; Marotta A; Salh B
CORPORATE SOURCE: The Department of Experimental Medicine, Jack Bell Research Center, University of British Columbia, 2660 Oak Street, Vancouver, British Columbia V6H 3Z6, Canada.
SOURCE: Oncogene, (2001 Oct 25) 20 (48) 6994-7005.
Journal code: 8711562. ISSN: 0950-9232.
PUB. COUNTRY: England: United Kingdom
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 200112
ENTRY DATE: Entered STN: 20011115
Last Updated on STN: 20020502
Entered Medline: 20011207

AB p53 undergoes phosphorylation on several residues in response to cellular stresses that include UV and ionizing radiation, however the influence of spindle damage on this parameter is relatively unclear. Consequently, the effect of nocodazole on **serine** 392 phosphorylation was examined in two epithelial cell lines. We show that this process is dependent upon the stepwise activation of p38 mitogen-activated protein **kinase** (p38 MAPK) and protein **kinase** casein **kinase** 2 (CK2). Furthermore, this activation correlated with the biochemical regulation of the maturation-promoting factor (MPF, cdc2/cyclin B), as both DRB and antisense depletion of CK2, as well as SB203580 were associated with an inhibition of its activation in response to nocodazole. Strikingly, when the cell cycle characteristics of nocodazole treated cells were examined, we observed that depletion or inhibition of the catalytic subunit of CK2, in the presence of microtubule inhibitors, resulted in a compromise of the G2 arrest (spindle checkpoint). Furthermore, CK2-depleted, nocodazole treated cells demonstrated a dramatic reduction in the apoptotic cell fraction, confirming that these cells had been endowed with oncogenic properties. These changes were observed in both HeLa cells and HCT116 cells. We also show that this effect is dependent on the presence of functional wild-type p53, as this phenomenon is not apparent in HCT116 p53(-/-) cells. Collectively, our results indicate two novel roles for CK2 in the spindle checkpoint arrest, in concert with p53. Firstly, to maintain increased cyclinB/cdc2 **kinase** activity, as a component of G2 arrest, and secondly, a role in p53-mediated apoptosis. These findings may have implications for an improved understanding of abnormalities of the spindle checkpoint in **human** cancers, which is a prerequisite for defining future therapies.

L9 ANSWER 22 OF 63 MEDLINE on STN
ACCESSION NUMBER: 2001561013 MEDLINE
DOCUMENT NUMBER: PubMed ID: 11607034
TITLE: Forkhead transcription factors contribute to execution of the mitotic programme in mammals.
AUTHOR: Alvarez B; Martinez-A C; Burgering B M; Carrera A C
CORPORATE SOURCE: Department of Immunology and Oncology, Centro Nacional de Biotecnologia, Consejo Superior de Investigaciones Cientificas, Universidad Autonoma de Madrid, Cantoblanco, Madrid E-28049, Spain.
SOURCE: Nature, (2001 Oct 18) 413 (6857) 744-7. Journal code: 0410462. ISSN: 0028-0836.
PUB. COUNTRY: England: United Kingdom
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 200112
ENTRY DATE: Entered STN: 20011022
Last Updated on STN: 20020420
Entered Medline: 20011205

AB Cell cycle progression is a process that is tightly controlled by internal and external signals. Environmental cues, such as those provided by growth factors, activate early signals that promote cell cycle entry. Cells that have progressed past the restriction point become independent of growth factors, and cell cycle progression is then controlled endogenously. The phosphatidylinositol 3OH **kinase** (PI(3)K)/protein **kinase** B (PKB) pathway must be activated in G1 to inactivate forkhead transcription factors (FKH-TFs) and allow cell cycle entry. Here we show that subsequent attenuation of the PI(3)K/PKB pathway is required to allow transcriptional activation of FKH-TF in G2. FKH-TF activity in G2 controls mammalian cell cycle termination, as interference with FKH transcriptional activation by disrupting PI(3)K/PKB downregulation, or by **expressing** a transcriptionally inactive FKH mutant, induces cell accumulation in G2/M, defective cytokinesis, and delayed transition from M to G1 of the cell cycle. We demonstrate that

FKH-TFs regulate **expression** of mitotic genes such as cyclin B and polo-like **kinase** (Plk). Our results support the important role of forkhead in the control of mammalian cell cycle completion, and suggest that efficient execution of the mitotic programme depends on downregulation of PI(3)K/PKB and consequent induction of FKH transcriptional activity.

L9 ANSWER 23 OF 63 MEDLINE on STN
ACCESSION NUMBER: 2001337489 MEDLINE
DOCUMENT NUMBER: PubMed ID: 11137007
TITLE: Xenopus ATR is a replication-dependent chromatin-binding protein required for the DNA replication checkpoint.
AUTHOR: Hekmat-Nejad M; You Z; Yee M C; Newport J W; Cimprich K A
CORPORATE SOURCE: Department of Molecular Pharmacology, Stanford University, Palo Alto, California 94305-5174, USA.
CONTRACT NUMBER: GM 33523 (NIGMS)
SOURCE: Current biology : CB, (2000 Dec 14-28) 10 (24) 1565-73. Journal code: 9107782. ISSN: 0960-9822.
PUB. COUNTRY: England: United Kingdom
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
OTHER SOURCE: GENBANK-AF320125
ENTRY MONTH: 200106
ENTRY DATE: Entered STN: 20010618
Last Updated on STN: 20010618
Entered Medline: 20010614

AB BACKGROUND: The DNA replication checkpoint ensures that mitosis is not initiated before DNA synthesis is completed. Recent studies using Xenopus extracts have demonstrated that activation of the replication checkpoint and phosphorylation of the Chk1 **kinase** are dependent on RNA primer synthesis by DNA polymerase alpha, and it has been suggested that the ATR **kinase**-so-called because it is related to the product of the gene that is mutated in ataxia telangiectasia (ATM) and to Rad3 **kinase**-may be an upstream component of this response. It has been difficult to test this hypothesis as an ATR-deficient system suitable for biochemical studies has not been available. RESULTS: We have **cloned** the Xenopus laevis homolog of ATR (XATR) and studied the function of the protein in Xenopus egg extracts. Using a chromatin-binding assay, we found that ATR associates with chromatin after initiation of replication, dissociates from chromatin upon completion of replication, and accumulates in the presence of aphidicolin, an inhibitor of DNA replication. Its association with chromatin was inhibited by treatment with actinomycin D, an inhibitor of RNA primase. There was an early rise in the activity of Cdc2-cyclin B in egg extracts depleted of ATR both in the presence or absence of aphidicolin. In addition, the premature mitosis observed upon depletion of ATR was accompanied by the loss of Chk1 phosphorylation. CONCLUSIONS: ATR is a replication-dependent chromatin-binding protein, and its association with chromatin is dependent on RNA synthesis by DNA polymerase alpha. Depletion of ATR leads to premature mitosis in the presence and absence of aphidicolin, indicating that ATR is required for the DNA replication checkpoint.

L9 ANSWER 24 OF 63 MEDLINE on STN
ACCESSION NUMBER: 2001140466 MEDLINE
DOCUMENT NUMBER: PubMed ID: 11146619
TITLE: DAP **kinase** activates a p19ARF/p53-mediated apoptotic checkpoint to suppress oncogenic transformation.
AUTHOR: Raveh T; Droguett G; Horwitz M S; DePinho R A; Kimchi A
CORPORATE SOURCE: Department of Molecular Genetics, Weizmann Institute of Science, Rehovot 76100, Israel.
SOURCE: Nature cell biology, (2001 Jan) 3 (1) 1-7. Journal code: 100890575. ISSN: 1465-7392.

PUB. COUNTRY: England: United Kingdom
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 200103
ENTRY DATE: Entered STN: 20010404
Last Updated on STN: 20010404
Entered Medline: 20010308

AB DAP **kinase** is a pro-apoptotic calcium-regulated **serine /threonine kinase**, whose **expression** is frequently lost in **human** tumours. Here we show that DAP **kinase** counteracts oncogene-induced transformation by activating a p19ARF/p53-dependent apoptotic checkpoint. Ectopic **expression** of DAP **kinase** suppressed oncogenic transformation of primary embryonic fibroblasts by activating p53 in a p19ARF-dependent manner. Consequently, the fibroblasts underwent apoptosis, characterized by caspase activation and DNA fragmentation. In response to c-Myc or E2F-1, the endogenous DAP **kinase** protein was upregulated. Furthermore, functional or genetic inactivation of the endogenous DAP **kinase** reduced the extent of induction of p19ARF/p53 and weakened the subsequent apoptotic responses to c-Myc or E2F-1. These results establish a role for DAP **kinase** in an early apoptotic checkpoint designed to eliminate pre-malignant cells during cancer development.

L9 ANSWER 25 OF 63 MEDLINE on STN
ACCESSION NUMBER: 2000496014 MEDLINE
DOCUMENT NUMBER: PubMed ID: 10862766
TITLE: Zipper-mediated oligomerization of the mixed lineage **kinase** SPRK/MLK-3 is not required for its activation by the GTPase **cdc** 42 but Is necessary for its activation of the JNK pathway. Monomeric SPRK L410P does not catalyze the activating phosphorylation of Thr258 of murine MITOGEN-ACTIVATED protein **kinase** **kinase** 4.
AUTHOR: Vacratsis P O; Gallo K A
CORPORATE SOURCE: Departments of Biochemistry and Physiology, Michigan State University, East Lansing, Michigan 48824, USA.
CONTRACT NUMBER: CA76306 (NCI)
SOURCE: Journal of biological chemistry, (2000 Sep 8) 275 (36) 27893-900.
Journal code: 2985121R. ISSN: 0021-9258.
PUB. COUNTRY: United States
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 200010
ENTRY DATE: Entered STN: 20001027
Last Updated on STN: 20020420
Entered Medline: 20001013

AB Src homology 3 domain-containing proline-rich **kinase** (SPRK)/mixed lineage **kinase**-3 is a **serine/ threonine kinase** that has been identified as an upstream activator of the c-Jun NH(2)-terminal **kinase** (JNK) pathway. SPRK is capable of activating MKK4 by phosphorylation of **serine** and **threonine** residues, and mutant forms of MKK4 that lack the phosphorylation sites Ser(254) and Thr(258) block SPRK-induced JNK activation. A region of 63 amino acids following the **kinase** domain of SPRK is predicted to form a leucine zipper. The leucine zipper domain of SPRK has been shown to be necessary and sufficient for SPRK oligomerization, but its role in regulating activation of SPRK and downstream signaling remains unclear. In this study, we substituted a proposed stabilizing leucine residue in the zipper domain with a helix-disrupting proline to abrogate zipper-mediated SPRK oligomerization.

We demonstrate that constitutively activated Cdc42 fully activates this monomeric SPRK mutant in terms of both autophosphorylation and histone phosphorylation activity and induces the same in vivo phosphorylation pattern as wild type SPRK. However, this catalytically active SPRK zipper mutant is unable to activate JNK. Our data show that the monomeric SPRK mutant fails to phosphorylate one of the two activating phosphorylation sites, Thr(258), of MKK4. These studies suggest that zipper-mediated SPRK oligomerization is not required for SPRK activation by Cdc42 but instead is critical for proper interaction and phosphorylation of a downstream target, MKK4.

L9 ANSWER 26 OF 63 MEDLINE on STN
ACCESSION NUMBER: 2000480464 MEDLINE
DOCUMENT NUMBER: PubMed ID: 10997979
TITLE: Lineage-specific regulation of cell cycle control gene **expression** during haematopoietic cell differentiation.
AUTHOR: Furukawa Y; Kikuchi J; Nakamura M; Iwase S; Yamada H; Matsuda M
CORPORATE SOURCE: Division of Molecular Haematopoiesis, Centre for Molecular Medicine, and Department of Haematology, Jichi Medical School, Tochigi, Japan.. furuyu@jichi.ac.jp
SOURCE: British journal of haematology, (2000 Sep) 110 (3) 663-73. Journal code: 0372544. ISSN: 0007-1048.
PUB. COUNTRY: ENGLAND: United Kingdom
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 200010
ENTRY DATE: Entered STN: 20001019
Last Updated on STN: 20001019
Entered Medline: 20001010

AB To maintain the fidelity and integrity of blood formation, the cell cycle is under strict regulation during haematopoietic cell differentiation. To elucidate the molecular mechanisms of cell cycle regulation during haematopoiesis, we examined cell cycle control gene **expression** during lineage-specific differentiation from CD34+ progenitor cells. **Expression** of cyclin-dependent **kinases** (cdks) and cyclins, except cdk4, was generally suppressed in CD34+ cells freshly isolated from the bone marrow of healthy volunteers. Among four major cdk inhibitors, p16 was **expressed** more highly in CD34+ cells than in CD34-negative bone marrow mononuclear cells, whereas the amounts of p21 and p27 transcripts increased in the CD34- population. The behaviour of cell cycle control genes during haematopoietic differentiation was classified into four patterns: (i) universal upregulation (cdc2, cdk2, cyclin A, cyclin B and p21); (ii) upregulation in specific lineages (cyclin D1, cyclin D3 and p15); (iii) no induction or stable **expression** (cdk4, cyclin D2, cyclin E and p27); and (iv) universal downregulation (p16). Lineage-specific changes included the sustained elevation of cdc2 and cyclin A during erythroid differentiation, cyclin D1 and p15 induction in myeloid lineage and selective upregulation of cyclin D3 in megakaryocytes. Blocking induction of cyclin D3 resulted in the inhibition of megakaryocytic differentiation. These results suggest that the **expression** of cell cycle control genes is distinctively regulated in a lineage-dependent manner, reflecting the cell cycle characteristics of each lineage. Some of these genes play an essential role in the process of differentiation itself.

L9 ANSWER 27 OF 63 MEDLINE on STN
ACCESSION NUMBER: 2000146287 MEDLINE
DOCUMENT NUMBER: PubMed ID: 10679924
TITLE: PRK, a cell cycle gene localized to 8p21, is downregulated in head and neck cancer.

AUTHOR: Dai W; Li Y; Ouyang B; Pan H; Reissmann P; Li J; Wiest J; Stambrook P; Gluckman J L; Noffsinger A; Bejarano P
CORPORATE SOURCE: Division of Hematology/Oncology, Department of Internal Medicine, University of Cincinnati College of Medicine, Cincinnati, Ohio 45267, USA.. wei.dai@uc.edu
CONTRACT NUMBER: RO1CA74299 (NCI)
SOURCE: Genes, chromosomes & cancer, (2000 Mar) 27 (3) 332-6.
Journal code: 9007329. ISSN: 1045-2257.
PUB. COUNTRY: United States
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 200003
ENTRY DATE: Entered STN: 20000320
Last Updated on STN: 20020420
Entered Medline: 20000309

AB The **human** PRK gene encodes a protein **serine/threonine kinase** of the polo family and plays an essential role in regulating meiosis and mitosis. We have previously shown that PRK **expression** is downregulated in a significant fraction of lung carcinomas. Our current studies reveal that PRK mRNA **expression** is downregulated in a majority (26 out of 35 patients) of primary head and neck squamous-cell carcinomas (HNSCC) compared with adjacent uninvolved tissues from the same patients, regardless of stage. In addition, PRK transcripts were undetectable in one of the two HNSCC cell lines analyzed. Ectopic **expression** of PRK, but not a PRK deletion construct, in transformed A549 fibroblast cells suppresses their proliferation. Furthermore, fluorescence in situ hybridization analyses show that the PRK gene localizes to chromosome band 8p21, a region that exhibits a high frequency of loss of heterozygosity in a variety of **human** cancers, including head and neck cancers, and that is proposed to contain two putative tumor suppressor genes. Considering that PRK plays an important role in the regulation of the G2/M transition and cell cycle progression, our current studies suggest that deregulated **expression** of PRK may contribute to tumor development. Genes Chromosomes Cancer 27:332-336, 2000.
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L9 ANSWER 28 OF 63 MEDLINE on STN
ACCESSION NUMBER: 2000145467 MEDLINE
DOCUMENT NUMBER: PubMed ID: 10679238
TITLE: **Human** p55(**CDC**)/Cdc20 associates with cyclin A and is phosphorylated by the cyclin A-Cdk2 complex.
AUTHOR: Ohtoshi A; Maeda T; Higashi H; Ashizawa S; Hatakeyama M
CORPORATE SOURCE: Department of Viral Oncology, Cancer Institute, Japanese Foundation for Cancer Research, Tokyo, 170-8455, Japan.
SOURCE: Biochemical and biophysical research communications, (2000 Feb 16) 268 (2) 530-4.
Journal code: 0372516. ISSN: 0006-291X.
PUB. COUNTRY: United States
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 200003
ENTRY DATE: Entered STN: 20000327
Last Updated on STN: 20021008
Entered Medline: 20000310

AB The initiation of anaphase and exit from mitosis depend on the activation of the anaphase-promoting complex/cyclosome (APC/C), a multicomponent, ubiquitin-protein ligase. The WD-repeat protein called p55(**CDC**)(Cdc20) directly binds to and activates APC/C. By using yeast two-hybrid screening, we found that cyclin A, a critical cell cycle regulator in the

S and G2/M phases, specifically interacts with p55(**CDC**). Ectopically **expressed** p55(**CDC**) and cyclin A form a stable protein complex in mammalian cells. The p55(**CDC**)-cyclin A interaction occurs through the region containing the WD repeats of p55(**CDC**) and the region between the destruction box and the cyclin box of cyclin A. In addition to the physical interaction, p55(**CDC**) is phosphorylated by cyclin A-associated **kinase**. These findings suggest that the function of p55(**CDC**) is mediated or regulated by its complex formation with cyclin A.
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L9 ANSWER 29 OF 63 MEDLINE on STN
ACCESSION NUMBER: 1999443781 MEDLINE
DOCUMENT NUMBER: PubMed ID: 10512862
TITLE: Requirement of sequences outside the conserved **kinase** domain of fission yeast Rad3p for checkpoint control.
AUTHOR: Chapman C R; Evans S T; Carr A M; Enoch T
CORPORATE SOURCE: Department of Genetics, Harvard Medical School, Boston, Massachusetts 02115, USA.
CONTRACT NUMBER: GM50015 (NIGMS)
SOURCE: Molecular biology of the cell, (1999 Oct) 10 (10) 3223-38. Journal code: 9201390. ISSN: 1059-1524.
PUB. COUNTRY: United States
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 199912
ENTRY DATE: Entered STN: 20000113
Last Updated on STN: 20000113
Entered Medline: 19991202
AB The fission yeast Rad3p checkpoint protein is a member of the phosphatidylinositol 3-**kinase**-related family of protein **kinases**, which includes **human** ATMp. Mutation of the ATM gene is responsible for the disease ataxia-telangiectasia. The **kinase** domain of Rad3p has previously been shown to be essential for function. Here, we show that although this domain is necessary, it is not sufficient, because the isolated **kinase** domain does not have **kinase** activity in vitro and cannot complement a rad3 deletion strain. Using dominant negative alleles of rad3, we have identified two sites N-terminal to the conserved **kinase** domain that are essential for Rad3p function. One of these sites is the putative leucine zipper, which is conserved in other phosphatidylinositol 3-**kinase**-related family members. The other is a novel motif, which may also mediate Rad3p protein-protein interactions.

L9 ANSWER 30 OF 63 MEDLINE on STN
ACCESSION NUMBER: 1998202387 MEDLINE
DOCUMENT NUMBER: PubMed ID: 9543386
TITLE: C-TAK1 protein **kinase** phosphorylates **human** Cdc25C on **serine** 216 and promotes 14-3-3 protein binding.
AUTHOR: Peng C Y; Graves P R; Ogg S; Thoma R S; Byrnes M J 3rd; Wu Z; Stephenson M T; Piwnica-Worms H
CORPORATE SOURCE: Department of Cell Biology and Physiology, Washington University School of Medicine, St. Louis, Missouri 63110, USA.
CONTRACT NUMBER: GM18428 (NIGMS)
GM47017 (NIGMS)
SOURCE: Cell growth & differentiation : molecular biology journal of the American Association for Cancer Research, (1998 Mar) 9 (3) 197-208. Journal code: 9100024. ISSN: 1044-9523.

PUB. COUNTRY: United States
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
OTHER SOURCE: GENBANK-U64205
ENTRY MONTH: 199805
ENTRY DATE: Entered STN: 19980520
Last Updated on STN: 20020420
Entered Medline: 19980514

AB Cdc25C is a dual-specificity protein **kinase** that controls entry into mitosis by dephosphorylating Cdc2 on both **threonine** 14 and tyrosine 15. Cdc25C is phosphorylated on **serine** 216 throughout interphase but not during mitosis. **Serine** 216 phosphorylation mediates the binding of 14-3-3 protein to Cdc25C, and Cdc25C/14-3-3 complexes are present throughout interphase but not during mitosis. Here we report the **cloning** of a **human kinase** denoted C-TAK1 (for **Cdc** twenty-five C associated protein **kinase**) that phosphorylates Cdc25C on **serine** 216 in vitro. C-TAK1 is ubiquitously **expressed** in **human** tissues and cell lines and is distinct from the DNA damage checkpoint **kinase** Chk1, shown previously to phosphorylate Cdc25C on **serine** 216. Cotransfection of Cdc25C with C-TAK1 resulted in enhanced phosphorylation of Cdc25C on **serine** 216. In addition, a physical interaction between C-TAK1 and Cdc25C was observed upon transient overexpression in COS-7 cells. Finally, coproduction of Cdc25C and C-TAK1 in bacteria resulted in the stoichiometric phosphorylation of Cdc25C on **serine** 216 and facilitated 14-3-3 protein binding in vitro. Taken together, these results suggest that one function of C-TAK1 may be to regulate the interactions between Cdc25C and 14-3-3 in vivo by phosphorylating Cdc25C on **serine** 216.

L9 ANSWER 31 OF 63 MEDLINE on STN
ACCESSION NUMBER: 1998070749 MEDLINE
DOCUMENT NUMBER: PubMed ID: 9405610
TITLE: Identification and characterization of a **human** protein **kinase** related to budding yeast Cdc7p.
AUTHOR: Jiang W; Hunter T
CORPORATE SOURCE: Molecular Biology and Virology Laboratory, The Salk Institute, 10010 North Torrey Pines Road, La Jolla, CA 92037, USA.. wjiang@axpl.salk.edu
CONTRACT NUMBER: CA14195 (NCI)
CA39780 (NCI)
SOURCE: Proceedings of the National Academy of Sciences of the United States of America, (1997 Dec 23) 94 (26) 14320-5. Journal code: 7505876. ISSN: 0027-8424.
PUB. COUNTRY: United States
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
OTHER SOURCE: GENBANK-AF005209
ENTRY MONTH: 199802
ENTRY DATE: Entered STN: 19980217
Last Updated on STN: 19980217
Entered Medline: 19980202

AB The Cdc7p protein **kinase** is essential for the G1/S transition and initiation of DNA replication during the cell division cycle in Saccharomyces cerevisiae. Cdc7p appears to be an evolutionarily conserved protein, since a homolog Hsk1 has been isolated from Schizosaccharomyces pombe. Here, we report the isolation of a **human** cDNA, HsCdc7, whose product is closely related in sequence to Cdc7p and Hsk1. The HsCdc7 cDNA encodes a protein of 574 amino acids with predicted size of 64 kDa. HsCdc7 contains the conserved subdomains common to all protein-**serine/threonine kinases** and three "

kinase inserts" that are characteristic of Cdc7p and Hsk1. Immune complexes of HsCdc7 from cell lysates were able to phosphorylate histone H1 in vitro. Indirect immunofluorescence staining demonstrated that HsCdc7 protein was predominantly localized in the nucleus. Although the **expression** levels of HsCdc7 appeared to be constant throughout the cell cycle, the protein **kinase** activity of HsCdc7 increased during S phase of the cell cycle at approximately the same time as that of Cdk2. These results, together with the functions of Cdc7p in yeast, suggest that HsCdc7 may phosphorylate critical substrate(s) that regulate the G1/S phase transition and/or DNA replication in mammalian cells.

L9 ANSWER 32 OF 63 MEDLINE on STN
ACCESSION NUMBER: 96310353 MEDLINE
DOCUMENT NUMBER: PubMed ID: 8744945
TITLE: Distinct roles of yeast MEC and RAD checkpoint genes in transcriptional induction after DNA damage and implications for function.
AUTHOR: Kiser G L; Weinert T A
CORPORATE SOURCE: Molecular and Cellular Biology Department, University of Arizona, Tucson 85721, USA.
CONTRACT NUMBER: R01-GM45276-05 (NIGMS)
SOURCE: Molecular biology of the cell, (1996 May) 7 (5) 703-18. Journal code: 9201390. ISSN: 1059-1524.
PUB. COUNTRY: United States
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 199703
ENTRY DATE: Entered STN: 19970321
Last Updated on STN: 20020907
Entered Medline: 19970307

AB In eukaryotic cells, checkpoint genes cause arrest of cell division when DNA is damaged or when DNA replication is blocked. In this study of budding yeast checkpoint genes, we identify and characterize another role for these checkpoint genes after DNA damage-transcriptional induction of genes. We found that three checkpoint genes (of six genes tested) have strong and distinct roles in transcriptional induction in four distinct pathways of regulation (each defined by induction of specific genes). MEC1 mediates the response in three transcriptional pathways, RAD53 mediates two of these pathways, and RAD17 mediates but a single pathway. The three other checkpoint genes (including RAD9) have small (twofold) but significant roles in transcriptional induction in all pathways. One of the pathways that we identify here leads to induction of MEC1 and RAD53 checkpoint genes themselves. This suggests a positive feedback circuit that may increase the cell's ability to respond to DNA damage. We make two primary conclusions from these studies. First, MEC1 appears to be the key regulator because it is required for all responses (both transcriptional and cell cycle arrest), while other genes serve only a subset of these responses. Second, the two types of responses, transcriptional induction and cell cycle arrest, appear distinct because both require MEC1 yet only cell cycle arrest requires RAD9. These and other results were used to formulate a working model of checkpoint gene function that accounts for roles of different checkpoint genes in different responses and after different types of damage. The conclusion that the yeast MEC1 gene is a key regulator also has implications for the role of a putative **human** homologue, the ATM gene.

L9 ANSWER 33 OF 63 MEDLINE on STN
ACCESSION NUMBER: 93234536 MEDLINE
DOCUMENT NUMBER: PubMed ID: 8475104
TITLE: Temporal regulation of cyclin A-p107 and p33cdk2 complexes binding to a **human** thymidine **kinase** promoter element important for G1-S phase transcriptional

regulation.
AUTHOR: Li L J; Naeve G S; Lee A S
CORPORATE SOURCE: Department of Biochemistry, University of Southern California School of Medicine, Los Angeles 90033.
CONTRACT NUMBER: GM31138 (NIGMS)
SOURCE: Proceedings of the National Academy of Sciences of the United States of America, (1993 Apr 15) 90 (8) 3554-8. Journal code: 7505876. ISSN: 0027-8424.
PUB. COUNTRY: United States
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 199305
ENTRY DATE: Entered STN: 19930604
Last Updated on STN: 19980206
Entered Medline: 19930517

AB The cyclins are an extensive family of proteins whose cell cycle-dependent synthesis is postulated to control multiple events during the cell cycle. The synthesis of A-type cyclins begins at the start of S phase. In mammalian cells, association with the **cdc**-type **kinases** suggests that cyclin A complexes are important for DNA replication and regulating other DNA-bound substrates required for S phase. We report here that a 25-bp promoter element previously shown to be important for the G1-S activation of the **human** thymidine **kinase** (htk) promoter in growth-stimulated cells is a cellular target of cyclin A and the p33cdk2 complexes. Though the p33cdk2 and other nuclear factor complexes exhibit constitutive binding to the htk G1-S regulatory domain, the binding activity of a cyclin A/p107 protein complex is greatly enhanced when the cells enter S phase, correlating with the increase in the tk mRNA levels and the replication of DNA. The binding activity of the cyclin A complex is maintained throughout S phase. Mutation of the DNA sequences on either half of the 25-bp protein binding site results in the loss of its ability to compete efficiently in vitro for the htk complexes, including that of cyclin A-containing complex. The loss of high-affinity binding for the htk complexes also substantially reduces the S-phase regulation of the htk promoter in vivo. Our results support the hypothesis that a cyclin A complex, in association with the p33cdk2 **kinase**, mediates the S-phase-regulated transcription of the htk promoter in growth-stimulated cells.

L9 ANSWER 34 OF 63 MEDLINE on STN
ACCESSION NUMBER: 91197455 MEDLINE
DOCUMENT NUMBER: PubMed ID: 2085430
TITLE: Protein **kinase** cascades in meiotic and mitotic cell cycle control.
AUTHOR: Pelech S L; Sanghera J S; Daya-Makin M
CORPORATE SOURCE: Biomedical Research Centre, University of British Columbia, Vancouver, Canada.
SOURCE: Biochemistry and cell biology = Biochimie et biologie cellulaire, (1990 Dec) 68 (12) 1297-330. Ref: 436 Journal code: 8606068. ISSN: 0829-8211.
PUB. COUNTRY: Canada
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
General Review; (REVIEW)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 199105
ENTRY DATE: Entered STN: 19910607
Last Updated on STN: 19970203
Entered Medline: 19910523

AB Eukaryotic cell cycle progression during meiosis and mitosis is extensively regulated by reversible protein phosphorylation. Many cell surface receptors for mitogens are ligand-stimulated protein-tyrosine

kinases that control the activation of a network of cytoplasmic and nuclear protein-**serine (threonine) kinases**. Over 30 plasma membrane associated protein-tyrosine **kinases** are encoded by proto-oncogenes, i.e., genes that have the potential to facilitate cancer when disregulated. Proteins such as ribosomal protein S6, microtubule-associated protein-2, myelin basic protein, and casein have been used to detect intracellular protein-**serine (threonine) kinases** that are activated further downstream in growth factor signalling transduction cascades. Genetic analysis of yeast cell division control (**cdc**) mutants has revealed another 20 or so protein-**serine (threonine) kinases**. One of these, specified by the **cdc**-2 gene in Schizosaccharomyces pombe, has homologs that are stimulated during M phase in maturing sea star and frog oocytes and mammalian somatic cells. Furthermore, during meiotic maturation in these echinoderm and amphibian oocytes, this is followed by activation of many of the same protein-**serine (threonine) kinases** that are stimulated when quiescent mammalian somatic cells are prompted with mitogens to traverse from G0 to G1 phase. These findings imply that a similar protein **kinase** cascade may oversee progression at multiple points in the cell cycle.

L9 ANSWER 35 OF 63 MEDLINE on STN
ACCESSION NUMBER: 91139618 MEDLINE
DOCUMENT NUMBER: PubMed ID: 1704889
TITLE: Molecular **cloning** of a novel **human** cdc2/CDC28-like protein **kinase**.
AUTHOR: Johnson K W; Smith K A
CORPORATE SOURCE: Department of Medicine, Dartmouth Medical School, Hanover, New Hampshire 03756.
SOURCE: Journal of biological chemistry, (1991 Feb 25) 266 (6) 3402-7.
Journal code: 2985121R. ISSN: 0021-9258.
PUB. COUNTRY: United States
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
OTHER SOURCE: GENBANK-D90240; GENBANK-D90266; GENBANK-M59287; GENBANK-M60913; GENBANK-M61894; GENBANK-M61895; GENBANK-M64401; GENBANK-M64402; GENBANK-M64485; GENBANK-M64590
ENTRY MONTH: 199103
ENTRY DATE: Entered STN: 19910412
Last Updated on STN: 19960129
Entered Medline: 19910327

AB A homology probing approach was utilized to isolate a new **human** protein **kinase**. Deoxyoligonucleotide probes recognizing a conserved subdomain in the COOH-terminal portion of protein **kinases** identified a cDNA **clone** encoding a putative **kinase** with predicted **serine/threonine** phosphorylation specificity. The full-length, 1.7-kilobase pair cDNA hybridizes to 1.7- and 3.4-kilobase mRNA transcripts in a number of tissues. The size of the encoded protein is 454 amino acids and consists of an NH2-terminal 130-residue segment, which may represent a regulatory region, followed by a 324-residue catalytic domain. Comparisons and alignments of the primary sequence and predicted secondary structure of the catalytic region to other known **kinases** reveal that the new **kinase**, denoted "CLK" (for **CDC**-like **kinase**), represents a prototype for a new family of **human** protein **kinases** bearing significant homology to the yeast cdc2/CDC28 **kinases** that regulate the cell cycle.

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ACCESSION NUMBER: 2003259427 EMBASE
TITLE: Caffeine induces G(2)/M arrest and apoptosis via a novel p53-dependent pathway in NB4 promyelocytic leukemia cells.
AUTHOR: Ito K.; Nakazato T.; Miyakawa Y.; Yamato K.; Ikeda Y.; Kizaki M.
CORPORATE SOURCE: M. Kizaki, Division of Hematology, Department of Internal Medicine, Keio University School of Medicine, 35 Shinanomachi, Shinjuku-ku, Tokyo 160-8582, Japan. makizaki@sc.itc.keio.ac.jp
SOURCE: Journal of Cellular Physiology, (1 Aug 2003) Vol. 196, No. 2, pp. 276-283.
Refs: 33
ISSN: 0021-9541 CODEN: JCLLAX
COUNTRY: United States
DOCUMENT TYPE: Journal; Article
FILE SEGMENT: 016 Cancer
LANGUAGE: English
SUMMARY LANGUAGE: English
ENTRY DATE: Entered STN: 20030717
Last Updated on STN: 20030717

AB Methylxantine derivative, caffeine, is known to prevent the p53-dependent apoptosis pathway via inhibition of ATM (ataxia telangiectasia mutated) **kinase**, which activates p53 by phosphorylation of the Ser-15 residue. In contrast, it has been reported that caffeine induces p53-mediated apoptosis through Bax protein in non-small-cell lung cancer cells. Therefore, the effects of caffeine on cellular growth in malignant cells are controversial. We investigated the effects of caffeine on cell proliferation, cell cycle progression, and induction of apoptosis in NB4 promyelocytic leukemia cells containing wild-type p53. Caffeine suppressed the cellular growth of NB4 cells in a dose- and time-dependent manner. Caffeine induced G(2)/M phase cell cycle arrest in NB4 cells in association with the induction of phosphorylation at the Ser-15 residue of p53 and induction of tyrosine phosphorylation of cdc2. **Expression** of Bax protein was increased in NB4 cells after treatment with caffeine. Interestingly, the antisense oligonucleotides for p53 significantly reduced p53 **expression** and caffeine-induced G(2)/M phase cell cycle arrest in NB4 cells. These results suggest that caffeine induces cell cycle arrest and apoptosis in association with activation of p53 by a novel pathway to phosphorylate the Ser-15 residue and induction of phosphorylation of **cdc** 2 in leukemic cells with normal p53.
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L9 ANSWER 37 OF 63 EMBASE COPYRIGHT 2005 ELSEVIER INC. ALL RIGHTS RESERVED. on STN
ACCESSION NUMBER: 1998013677 EMBASE
TITLE: Myotonic dystrophy **kinase**-related Cdc42-binding **kinase** acts as a Cdc42 effector in promoting cytoskeletal reorganization.
AUTHOR: Leung T.; Chen X.-Q.; Tan I.; Manser E.; Lim L.
CORPORATE SOURCE: L. Lim, Glaxo-IMCB Group, Institute of Molecular/Cell Biology, National University of Singapore, Kent Ridge 119260, Singapore. L.Lim@ion.ucl.ac.uk
SOURCE: Molecular and Cellular Biology, (1998) Vol. 18, No. 1, pp. 130-140.
Refs: 54
ISSN: 0270-7306 CODEN: MCEBD4
COUNTRY: United States
DOCUMENT TYPE: Journal; Article
FILE SEGMENT: 029 Clinical Biochemistry
LANGUAGE: English
SUMMARY LANGUAGE: English
ENTRY DATE: Entered STN: 19980205
Last Updated on STN: 19980205

AB The Rho GTPases play distinctive roles in cytoskeletal reorganization associated with growth and differentiation. The Cdc42/Rac-binding p21-activated **kinase** (PAK) and Rho-binding **kinase** (ROK) act as morphological effectors for these GTPases. We have isolated two related novel brain **kinases** whose p21-binding domains resemble that of PAK whereas the **kinase** domains resemble that of myotonic dystrophy **kinase**-related ROK. These .apprx.190-kDa myotonic dystrophy **kinase**-related Cdc42-binding **kinases** (MRCKs) preferentially phosphorylate nonmuscle myosin light chain at **serine** 19, which is known to be crucial for activating actin-myosin contractility. The p21- binding domain binds GTP-Cdc42 but not GDP-Cdc42. The multidomain structure includes a cysteine-rich motif resembling those of protein **kinase** C and n- chimaerin and a putative pleckstrin homology domain. MRCKα and Cdc42(V12) colocalize, particularly at the cell periphery in transfected HeLa cells. Microinjection of plasmid encoding MRCKα resulted in actin and myosin reorganization. **Expression** of **kinase**-dead MRCKα blocked Cdc42(V12)-dependent formation of focal complexes and peripheral microspikes. This was not due to possible sequestration of the p21, as a **kinase**-dead MRCKα mutant defective in Cdc42 binding was an equally effective blocker. Coinjection of MRCKα plasmid with Cdc42 plasmid, at concentrations where Cdc42 plasmid by itself elicited no effect, led to the formation of the peripheral structures associated with a Cdc42-induced morphological phenotype. These Cdc42-type effects were not promoted upon coinjection with plasmids of **kinase**-dead or Cdc42-binding-deficient MRCKα mutants. These results suggest that MRCKα may act as a downstream effector of Cdc42 in cytoskeletal reorganization.

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ACCESSION NUMBER: 2004:316263 BIOSIS
DOCUMENT NUMBER: PREV200400315861
TITLE: Manipulation of alternative splicing by a newly developed inhibitor of Clks.
AUTHOR(S): Muraki, Michiko; Ohkawara, Bisei; Hosoya, Takamitsu; Onogi, Hiroshi; Koizumi, Jun; Koizumi, Tomonobu; Sumi, Kengo; Yomoda, Jun-ichiro; Murray, Michael V.; Kimura, Hiroshi; Furuichi, Kiyoshi; Shibuya, Hiroshi; Krainer, Adrian R.; Suzuki, Masaaki; Hagiwara, Masatoshi [Reprint Author]
CORPORATE SOURCE: Sch Biomed SciGene Express LabBunkyo Ku, Tokyo Med and Dent Univ, 1-5-45 Yushima, Tokyo, 1138510, Japan
m.hagiwara.end@mri.tmd.ac.jp
SOURCE: Journal of Biological Chemistry, (June 4 2004) Vol. 279, No. 23, pp. 24246-24254. print.
CODEN: JBCHA3. ISSN: 0021-9258.
DOCUMENT TYPE: Article
LANGUAGE: English
ENTRY DATE: Entered STN: 15 Jul 2004
Last Updated on STN: 15 Jul 2004

AB The regulation of splice site usage provides a versatile mechanism for controlling gene **expression** and for the generation of proteome diversity, playing an essential role in many biological processes. The importance of alternative splicing is further illustrated by the increasing number of **human** diseases that have been attributed to mis-splicing events. Appropriate spatial and temporal generation of splicing variants demands that alternative splicing be subjected to extensive regulation, similar to transcriptional control. The Clk (Cdc2-like **kinase**) family has been implicated in splicing control and consists of at least four members. Through extensive screening of a chemical library, we found that a benzothiazole compound, TG003, had a potent inhibitory effect on the activity of Clk1/Sty. TG003 inhibited SF2/ASF-dependent splicing of beta-globin pre-mRNA in vitro by

suppression of Clk-mediated phosphorylation. This drug also suppressed **serine**/arginine-rich protein phosphorylation, dissociation of nuclear speckles, and Clk1/Sty-dependent alternative splicing in mammalian cells. Consistently, administration of TG003 rescued the embryonic defects induced by excessive Clk activity in Xenopus. Thus, TG003, a novel inhibitor of Clk family will be a valuable tool to dissect the regulatory mechanisms involving **serine**/arginine-rich protein phosphorylation signaling pathways in vivo, and may be applicable for the therapeutic manipulation of abnormal splicing.

L9 ANSWER 39 OF 63 BIOSIS COPYRIGHT (c) 2005 The Thomson Corporation on STN

ACCESSION NUMBER: 2004:307337 BIOSIS
DOCUMENT NUMBER: PREV200400304614
TITLE: Mutation of a CK2 phosphorylation site in cdc25C impairs importin alpha/beta binding and results in cytoplasmic retention.
AUTHOR(S): Schwindling, Sandra L.; Noll, Andreas; Montenarh, Mathias; Goetz, Claudia [Reprint Author]
CORPORATE SOURCE: Univ Saarlandes, Gebaude 44, D-66421, Homburg, Germany bccgoe@uniklinik-saarland.de
SOURCE: Oncogene, (May 20 2004) Vol. 23, No. 23, pp. 4155-4165. print.
ISSN: 0950-9232 (ISSN print).
DOCUMENT TYPE: Article
LANGUAGE: English
ENTRY DATE: Entered STN: 7 Jul 2004
Last Updated on STN: 7 Jul 2004

AB cdc25C is a phosphatase, which activates the mitosis-promoting factor cyclin B1/cdc2 by dephosphorylation, and thus triggers G2/M transition. The activity of cdc25C itself is controlled by phosphorylation of certain amino-acid residues, which among other things determines the subcellular localization of the enzyme. Here, we describe a new phosphorylation site at **threonine** 236 of cdc25C, which is phosphorylated by protein **kinase** CK2. This phosphorylation site is located near the nuclear localization signal (amino acids 239 - 245). We demonstrate that cdc25C interacts with importin beta and the importin alpha/beta heterodimer but not with importin a. We further found that a cdc25C phosphorylation mutant where **threonine** 236 was replaced by aspartic acid as well as cdc25C phosphorylated by CK2 binds importin b or the importin alpha/beta heterodimer less efficiently than wild type or the corresponding alanine mutant. Furthermore, the cdc25CT236D shows a retarded uptake into the nucleus in a cell import assay. Inhibition of protein **kinase** CK2 enzyme activity in vivo resulted in an enhanced nuclear localization of cdc25C. Thus, phosphorylation of cdc25C at **threonine** 236 is an important signal for the retention of cdc25C in the cytoplasm.

L9 ANSWER 40 OF 63 BIOSIS COPYRIGHT (c) 2005 The Thomson Corporation on STN

ACCESSION NUMBER: 2004:187498 BIOSIS
DOCUMENT NUMBER: PREV200400190103
TITLE: Polo-like **kinase** 1 (PLK1) **expression** is associated with cell proliferative activity and Cdc2 **expression** in malignant lymphoma of the thyroid.
AUTHOR(S): Ito, Yasuhiro [Reprint Author]; Yoshida, Hiroshi; Matsuzuka, Fumio; Matsuura, Nariaki; Nakamura, Yasushi; Nakamine, Hirokazu; Kakudo, Kennichi; Kuma, Kanji; Miyauchi, Akira
CORPORATE SOURCE: Department of Surgery, Kuma Hospital, 8-2-35, Shimoyamate-dori, Chuo-ku, Kobe, 650-0011, Japan ito01@kuma-h.or.jp
SOURCE: Anticancer Research, (January-February 2004) Vol. 24, No.

1, pp. 259-264. print.
CODEN: ANTRD4. ISSN: 0250-7005.
DOCUMENT TYPE: Article
LANGUAGE: English
ENTRY DATE: Entered STN: 7 Apr 2004
Last Updated on STN: 7 Apr 2004

AB Background: Polo-like **kinase** 1 (PLK1) is one of the **serine threonine kinases** that plays a role in cellular proliferation by activating the CDC25C-CDKI (cdc2) loop. We recently demonstrated that cdc2 **expression** is associated with the biological aggressiveness of malignant lymphoma of the thyroid. In this study, we investigated PLK1 **expression** in thyroid lymphoma in order to elucidate its physiological significance in this disease. Materials and Methods: We immunohistochemically investigated PLK1 **expression** in 46 cases of thyroid lymphoma and 10 cases of chronic thyroiditis. Results: Normal follicular cells did not **express** PLK1, whereas follicular cells in those in chronic thyroiditis and malignant lymphoma demonstrated a high level of PLK1 **expression**. In lymphocytes in chronic thyroiditis with strong lymphocyte infiltration, PLK1 was weakly **expressed**. In malignant lymphoma, PLK1 **expression** was observed in all cases, but PLK1 was more strongly **expressed** in cases with high cell proliferative activity and with cdc2 **expression**. Conclusion: These results suggest that PLK1 regulates the cell cycle progression of thyroid lymphoma cells in the G2-M-phase.

L9 ANSWER 41 OF 63 BIOSIS COPYRIGHT (c) 2005 The Thomson Corporation on STN
ACCESSION NUMBER: 2004:150245 BIOSIS
DOCUMENT NUMBER: PREV200400146915
TITLE: Rituximab and 17-AAG synergistically induce apoptosis in B-cell chronic lymphocytic leukemia (CLL).
AUTHOR(S): Johnson, Amy J. [Reprint Author]; Eisenbeis, Charles F. [Reprint Author]; Cheney, Carolyn M. [Reprint Author]; Mone, Andrew P. [Reprint Author]; Lucas, David M. [Reprint Author]; Byrd, John C. [Reprint Author]
CORPORATE SOURCE: Internal Medicine, Ohio State University, Columbus, OH, USA
SOURCE: Blood, (November 16 2003) Vol. 102, No. 11, pp. 437a-438a. print.
Meeting Info.: 45th Annual Meeting of the American Society of Hematology. San Diego, CA, USA. December 06-09, 2003. American Society of Hematology.
CODEN: BLOOAW. ISSN: 0006-4971.
DOCUMENT TYPE: Conference; (Meeting)
Conference; (Meeting Poster)
Conference; Abstract; (Meeting Abstract)
LANGUAGE: English
ENTRY DATE: Entered STN: 17 Mar 2004
Last Updated on STN: 17 Mar 2004

AB Rituximab is an anti-CD20 monoclonal antibody that is clinically active in B-cell chronic lymphocytic leukemia (CLL). In vitro and in vivo data indicate that rituximab mediates its biologic effect through multiple mechanisms including apoptosis, complement dependent cytotoxicity (**CDC**), and antibody dependent cellular cytotoxicity (ADCC). Recent discoveries in our laboratory using anti-HLA-DR antibodies have illustrated the importance of signaling and survival pathways such as AKT in CLL. We have recently extended these studies to rituximab, demonstrating that addition of rituximab crosslinked with Ig Fc gamma fragment specific antibodies generates reactive oxygen species and activates AKT in vitro. We then hypothesized that AKT activation in part inhibits cell death signals induced by rituximab. The semisynthetic geldanamycin derivative 17-allylamino-17-demethoxygeldanamycin (17-AAG) binds to and inhibits the activity of the heat shock protein Hsp90, which

functions to stabilize important tyrosine and **serine** **kinases** such as c-src, Raf-1, and AKT. In vitro studies in several solid and hematologic tumor cell lines demonstrated the ability of 17-AAG to destabilize and deplete AKT in tumor cells. We therefore hypothesized that 17-AAG would be highly synergistic with rituximab. Our initial experiments with 17-AAG and rituximab in vitro in **human** CLL cells demonstrated that exposure to 10 uM 17-AAG for 24 or 48 hours decreased AKT **kinase** activity to background levels, thus confirming that 17-AAG was able to completely abrogate the cell survival signal generated through AKT. Tumor cells from three CLL patients were exposed to 1 uM 17-AAG and 10 ug/ml rituximab for 24 or 48 hours in culture. Apoptosis was examined by annexin V-FITC and propidium iodide staining, and AKT **expression** was examined by immunoblot. 17-AAG treatment alone resulted in 19% apoptosis after 24 hours (media alone <10%), whereas rituximab induced apoptosis in 27% of cells. However, the combination of 17-AAG and rituximab resulted in 49% apoptosis after 24 hours, and this effect was increased after 48 hours. Immunoblotting of cell lysates of tumor cells from CLL patients treated in vitro with 0.5 uM and 1 uM 17-AAG for 24 hours showed that 1 uM 17-AAG decreased AKT **expression** by 55%, compared to media alone in primary CLL cells. This reduction in AKT was observed in cells from all three CLL patients tested, although the magnitude of the decrease varied. Thus, preliminary in vitro data indicate that 17-AAG down-regulates the cell survival protein AKT and synergistically induces apoptosis with rituximab. 17-AAG did not affect the activity of natural killer cells against target Daudi cells, suggesting that ADCC is not involved in this process. Thus, our data suggest that combination of targeted therapies 17-AAG and rituximab represents a potentially powerful new therapeutic approach to CLL treatment.

L9 ANSWER 42 OF 63 BIOSIS COPYRIGHT (c) 2005 The Thomson Corporation on STN

ACCESSION NUMBER: 2001:397274 BIOSIS
DOCUMENT NUMBER: PREV200100397274
TITLE: CrkRS: A novel conserved Cdc2-related protein **kinase** that colocalises with SC35 speckles.
AUTHOR(S): Ko, Tun K.; Kelly, Emma; Pines, Jonathon [Reprint author]
CORPORATE SOURCE: Wellcome/CRC Institute, Tennis Court Road, Cambridge, CB2 1QR, UK
j.pines@welc.cam.ac.uk
SOURCE: Journal of Cell Science, (July, 2001) Vol. 114, No. 14, pp. 2591-2603. print.
CODEN: JNCSAI. ISSN: 0021-9533.
DOCUMENT TYPE: Article
LANGUAGE: English
ENTRY DATE: Entered STN: 22 Aug 2001
Last Updated on STN: 22 Feb 2002

AB We have isolated and characterised a novel **human** protein **kinase**, Cdc2-related **kinase** with an arginine/**serine**-rich (RS) domain (CrkRS), that is most closely related to the cyclin-dependent **kinase** (CDK) family. CrkRS is a 1490 amino acid protein, the largest CDK-related **kinase** so far isolated. The protein **kinase** domain of CrkRS is 89% identical to the 46 kDa CHED protein **kinase**, but outside the **kinase** domains the two proteins are completely unrelated. CrkRS has extensive proline-rich regions that match the consensus for SH3 and WW domain binding sites, and an RS domain that is predominantly found in splicing factors. CrkRS is ubiquitously **expressed** in tissues, and maps to a single genetic locus. There are closely related protein **kinases** in both the Drosophila and Caenorhabditis elegans genomes. Consistent with the presence of an RS domain, anti-CrkRS antibodies stain nuclei in a speckled pattern, overlapping with spliceosome components and the hyperphosphorylated form of RNA polymerase II. Like RNA polymerase

II, CrkRS is a constitutive MPM-2 antigen throughout the cell cycle. Anti-CrkRS immunoprecipitates phosphorylate the C-terminal domain of RNA polymerase II in vitro. Thus CrkRS may be a novel, conserved link between the transcription and splicing machinery.

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ACCESSION NUMBER: 2001:396033 BIOSIS
DOCUMENT NUMBER: PREV200100396033
TITLE: Multiple mechanisms regulate subcellular localization of **human** CDC6.
AUTHOR(S): Delmolino, Laurie M.; Saha, Partha; Dutta, Anindya [Reprint author]
CORPORATE SOURCE: Department of Pathology, Brigham and Women's Hospital, Harvard Medical School, Boston, MA, 02115, USA adutta@rics.bwh.harvard.edu
SOURCE: Journal of Biological Chemistry, (July 20, 2001) Vol. 276, No. 29, pp. 26947-26954. print.
CODEN: JBCHA3. ISSN: 0021-9258.
DOCUMENT TYPE: Article
LANGUAGE: English
ENTRY DATE: Entered STN: 22 Aug 2001
Last Updated on STN: 22 Feb 2002

AB CDC6 is a protein essential for DNA replication, the **expression** and abundance of which are cell cycle-regulated in Saccharomyces cerevisiae. We have demonstrated previously that the subcellular localization of the **human** CDC6 homolog, HsCDC6, is cell cycle-dependent: nuclear during G1 phase and cytoplasmic during S phase. Here we demonstrate that endogenous HsCDC6 is phosphorylated during the G1/S transition. The N-terminal region contains putative cyclin-dependent **kinase** phosphorylation sites adjoining nuclear localization sequences (NLSs) and a cyclin-docking motif, whereas the C-terminal region contains a nuclear export signal (NES). In addition, we show that the observed regulated subcellular localization depends on phosphorylation status, NLS, and NES. When the four putative substrate sites (**serines** 45, 54, 74, and 106) for cyclin-dependent **kinases** are mutated to alanines, the resulting HsCDC6A4 protein is localized predominantly to the nucleus. This localization depends upon two functional NLSs, because **expression** of HsCDC6 containing mutations in the two putative NLSs results in predominantly cytoplasmic distribution. Furthermore, mutation of the four **serines** to phosphate-mimicking aspartates (HsCDC6D4) results in strictly cytoplasmic localization. This cytoplasmic localization depends upon the C-terminal NES. Together these results demonstrate that HsCDC6 is phosphorylated at the G1/S phase of the cell cycle and that the phosphorylation status determines the subcellular localization.

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ACCESSION NUMBER: 2000:450052 BIOSIS
DOCUMENT NUMBER: PREV200000450052
TITLE: Different **kinases** phosphorylate nucleophosmin/B23 at different sites during G2 and M phases of the cell cycle.
AUTHOR(S): Jiang, Pei. S.; Chang, Jei. H.; Yung, Benjamin Y. M. [Reprint author]
CORPORATE SOURCE: Cancer Biochemistry Laboratory, Department of Pharmacology, College of Medicine, Chang Gung University, 259 Wen-Hwa 1st Road, Kwei-San, Tao-Yuan, 333, Taiwan
SOURCE: Cancer Letters, (May 29, 2000) Vol. 153, No. 1-2, pp. 151-160. print.
CODEN: CALEDQ. ISSN: 0304-3835.
DOCUMENT TYPE: Article

LANGUAGE: English
ENTRY DATE: Entered STN: 18 Oct 2000
Last Updated on STN: 10 Jan 2002

AB The **recombinant** GST-nucleophosmin/B23 and the truncated mutants were tested for phosphorylation in cell-free extracts of G2 and M phases or by purified **kinases**. Our results indicated that a **threonine** residue at amino acids (a.a) 185-240 was phosphorylated by cdc2 **kinase** during the entry of mitosis while the **serine** phosphorylation site at the middle acidic portion of the molecule (a.a. 83-152) was phosphorylated by casein **kinase** II during G2 phase. Our results also showed that there was possibly another **serine** phosphorylation at site other than the middle portion of nucleophosmin/B23 (a.a. 83-152) during the entry of cells into mitosis. The demonstration of the characteristic changes in phosphorylation of nucleophosmin/B23 during the cell cycle implicates important role of nucleophosmin/B23 in the control of the fate of nucleoli and cell growth.

L9 ANSWER 45 OF 63 BIOSIS COPYRIGHT (c) 2005 The Thomson Corporation on STN
ACCESSION NUMBER: 2000:396579 BIOSIS
DOCUMENT NUMBER: PREV200000396579
TITLE: Phosphorylation-dependent proline isomerization catalyzed by Pin1 is essential for tumor cell survival and entry into mitosis.
AUTHOR(S): Rippmann, Joerg F.; Hobbie, Silke; Daiber, Christine; Guilliard, Bernd; Bauer, Margit; Birk, Joachim; Nar, Herbert; Garin-Chesa, Pilar; Rettig, Wolfgang J.; Schnapp, Andreas [Reprint author]
CORPORATE SOURCE: Department of Oncology Research, Boehringer Ingelheim Pharma KG, Birkendorfer Strasse 65, 88397, Biberach an der Riss, Germany
SOURCE: Cell Growth and Differentiation, (July, 2000) Vol. 11, No. 7, pp. 409-416. print.
ISSN: 1044-9523.
DOCUMENT TYPE: Article
LANGUAGE: English
ENTRY DATE: Entered STN: 13 Sep 2000
Last Updated on STN: 8 Jan 2002

AB Pin1, a member of the parvulin family of peptidyl-prolyl cis-trans isomerases (PPIases) has been implicated in the G2-M transition of the mammalian cell cycle. Pin1 interacts with a series of mitotic phosphoproteins, including Polo-like **kinase**-1, Cdc25C, and Cdc27, and is thought to act as a phosphorylation-dependent PPIase for these target molecules. Pin1 recognizes phosphorylated **serine** -proline or **threonine**-proline peptide-bonds in test substrates up to 1300-fold better than in the respective unphosphorylated peptides. To test directly whether Pin1 regulates the G2-M transition and/or progression through mitosis by catalyzing phosphorylation-dependent prolyl isomerization of essential mitotic targets, we examined the consequences of Pin1 depletion, achieved by (a) overexpression of Pin1 antisense RNA, (b) overexpression of dominant-negative Pin1, and (c) by a known small-molecule Pin1-PPIase inhibitor, juglone. The results of all of the three lines of investigation show that the catalytic activity of Pin1 is essential for tumor cell survival and entry into mitosis.

L9 ANSWER 46 OF 63 BIOSIS COPYRIGHT (c) 2005 The Thomson Corporation on STN
ACCESSION NUMBER: 2000:387922 BIOSIS
DOCUMENT NUMBER: PREV200000387922
TITLE: Ste20-like **kinase** (SLK), a regulatory **kinase** for polo-like **kinase** (Plk) during the G2/M transition in somatic cells.
AUTHOR(S): Ellinger-Ziegelbauer, Heidrun; Karasuyama, Hajime; Yamada,

Eitaro; Tsujikawa, Kazutake; Todokoro, Kazuo; Nishida, Eisuke [Reprint author]
CORPORATE SOURCE: Department of Biophysics, Graduate School of Science, Kyoto University, Sakyo-ku, Kyoto, 606-8502, Japan
SOURCE: Genes to Cells, (June, 2000) Vol. 5, No. 6, pp. 491-498. print.
ISSN: 1356-9597.
DOCUMENT TYPE: Article
LANGUAGE: English
ENTRY DATE: Entered STN: 13 Sep 2000
Last Updated on STN: 8 Jan 2002

AB Background: Activation of the cyclin-dependent **kinase** cdc2-cyclin B1 at the G2/M transition of the cell cycle requires dephosphorylation of **threonine**-14 and tyrosine-15 in cdc2, which in higher eukaryotes is brought about by the Cdc25C phosphatase. In Xenopus, there is evidence that a **kinase** cascade comprised of xPlkk1 and Plx1, the Xenopus polo-like **kinase** 1, plays a key role in the activation of Cdc25C during oocyte maturation. In the mammalian somatic cell cycle, a polo-like **kinase** homologue (Plk1) also functions during mitosis, but a **kinase** upstream of Plk is still unknown. Results: We show here that **human** Ste20-like **kinase** (SLK), which is a ubiquitously **expressed** mammalian protein related to xPlkk1, can phosphorylate and activate murine Plk1. During progression through the G2 phase of the mammalian cell cycle, the activity of endogenous SLK is increased. The amount of SLK protein is decreased in quiescent and differentiating cells. Treatment with okadaic acid induces a phosphorylation-dependent enhancement of SLK activity. Conclusions: We propose that SLK has a role in the regulation of Plk1 activity in actively dividing cells during the somatic cell cycle. SLK itself is suggested to be regulated by phosphorylation.

L9 ANSWER 47 OF 63 BIOSIS COPYRIGHT (c) 2005 The Thomson Corporation on STN
ACCESSION NUMBER: 1999:135797 BIOSIS
DOCUMENT NUMBER: PREV199900135797
TITLE: A rate limiting function of cdc25A for S phase entry inversely correlates with tyrosine dephosphorylation of Cdk2.
AUTHOR(S): Sexl, Veronika; Diehl, J. Alan; Sherr, Charles J.; Ashmun, Richard; Beach, David; Roussel, Martine F. [Reprint author]
CORPORATE SOURCE: Dep. Tumor Cell Biol., St. Jude Children's Res. Hosp., Memphis, TN 38105, USA
SOURCE: Oncogene, (Jan., 1999) Vol. 18, No. 3, pp. 573-582. print.
CODEN: ONCNES. ISSN: 0950-9232.
DOCUMENT TYPE: Article
LANGUAGE: English
ENTRY DATE: Entered STN: 31 Mar 1999
Last Updated on STN: 31 Mar 1999

AB The cdc25A phosphatase removes inhibitory phosphates from **threonine**-14 and tyrosine-15 of cyclin dependent **kinase** -2 (cdk2) in vitro, and it is therefore widely assumed that cdc25A positively regulates cyclin E- and A-associated cdk2 activity at the G1 to S phase transition of the mammalian cell division cycle. **Human** cdc25A was introduced into mouse NIH3T3 fibroblasts co-**expressing** a form of the colony-stimulating factor-1 (CSF-1) receptor that is partially defective in transducing mitogenic signals. Cdc25A enabled these cells to form colonies in semisolid medium containing serum plus **human recombinant** CSF-1 in a manner reminiscent of cells rescued by c-myc. However, cdc25A-rescued cells could not proliferate in chemically defined medium containing CSF-1 and continued to require c-myc function for S phase entry. When contact-inhibited cells overexpressing cdc25A were dispersed and stimulated to synchronously enter the cell

division cycle, they entered S phase 2-3 h earlier than their parental untransfected counterparts. Shortening of G1 phase temporally correlated with more rapid degradation of the cdk inhibitor P27Kip1 and with premature activation of cyclin A-dependent cdk2. Paradoxically, tyrosine phosphorylation of cdk2 increased considerably as cells entered S phase, and cdc25A overexpression potentiated rather than diminished this effect. At face value, these results are inconsistent with the hypothesis that cdc25A acts directly on cdk2 to activate its S phase promoting function.

L9 ANSWER 48 OF 63 BIOSIS COPYRIGHT (c) 2005 The Thomson Corporation on STN

ACCESSION NUMBER: 1999:112185 BIOSIS
DOCUMENT NUMBER: PREV199900112185
TITLE: Functional association of TGF-beta receptor II with cyclin B.
AUTHOR(S): Liu, Jin Hong; Wei, Sheng; Burnette, Pearlie K.; Gamero, Ana M.; Hutton, Michael; Djeu, Julie Y. [Reprint author]
CORPORATE SOURCE: Immunology Program, H Lee Moffitt Cancer Center Research Institute, Dep. Biochemistry Molecular Biol., Univ. South Florida, Tampa, FL 33612, USA
SOURCE: Oncogene, (Jan. 7, 1999) Vol. 18, No. 1, pp. 269-275. print.
CODEN: ONCNES. ISSN: 0950-9232.
DOCUMENT TYPE: Article
LANGUAGE: English
ENTRY DATE: Entered STN: 12 Mar 1999
Last Updated on STN: 12 Mar 1999

AB Utilizing the cytoplasmic tail of Transforming Growth Factor Receptor Type II (TGFbeta RII) as bait in a yeast two hybrid system, we have identified **human** cyclin B2 as a direct physical partner of TGFbeta RII. Analysis of deletion mutants of glutathione-S-transferase (GST)-cyclin B2 mapped its binding domain for TGFbeta RII to the C-terminal and revealed a negative regulatory region immediately upstream of the cyclin box. Using **recombinant** proteins, Cdc2 was demonstrated to indirectly interact with TGFbeta RII via cyclin B2. This interaction was reproduced in THP-1 monocytic cells, where TGFbeta treatment markedly enhanced the ability of cyclin B2 and, correspondingly, Cdc2 from TGFbeta-treated THP-1 cells, to bind the GST-TGFbeta RII fusion protein. More importantly, TGFbeta RII co-precipitated with cyclin B2 in TGFbeta-treated THP-1 cells. TGFbeta treatment also caused **threonine** phosphorylation of Cdc2 in the TGFbeta RII-cyclin B2-Cdc2 complex in THP1 cells, in parallel with down regulation of Cdc2 function as measured by histone H1 **kinase** activity. Cyclin B1 had the same capacity to bind TGFbeta RII and mediate indirect Cdc2 binding. These results suggest an alternative mechanism that cell cycle arrest in the G1/S phase caused by TGFbeta may, in part, be due to inactivation of cyclin B/Cdc2 **kinase**, which is needed for entry into the G2/M phase.

L9 ANSWER 49 OF 63 BIOSIS COPYRIGHT (c) 2005 The Thomson Corporation on STN

ACCESSION NUMBER: 1998:179044 BIOSIS
DOCUMENT NUMBER: PREV199800179044
TITLE: C-TAK1 protein **kinase** phosphorylates **human** Cdc25C on **serine** 216 and promotes 14-3-3 protein binding.
AUTHOR(S): Peng, Cheng-Yuan; Graves, Paul R.; Ogg, Scott; Thoma, Richard S.; Byrnes, Michael J., III; Wu, Zhiqi; Stephenson, Mary T.; Piwnica-Worms, Helen [Reprint author]
CORPORATE SOURCE: Dep. Cell Biol. Physiol., Howard Hughes Med. Inst., Washington Univ. Sch. Med., Box 8228, 660 South Euclide Ave., St. Louis, MO 63110, USA
SOURCE: Cell Growth and Differentiation, (March, 1998) Vol. 9, No. 3, pp. 107-208. print.

ISSN: 1044-9523.
DOCUMENT TYPE: Article
LANGUAGE: English
ENTRY DATE: Entered STN: 20 Apr 1998
Last Updated on STN: 12 Aug 1998

AB Cdc25C is a dual-specificity protein **kinase** that controls entry into mitosis by dephosphorylating Cdc2 on both **threonine** 14 and tyrosine 15. Cdc25C is phosphorylated on **serine** 216 throughout interphase but not during mitosis. **Serine** 216 phosphorylation mediates the binding of 14-3-3 protein to Cdc25C, and Cdc25C/14-3-3 complexes are present throughout interphase but not during mitosis. Here we report the **cloning** of a **human kinase** denoted C-TAK1 (for **Cdc** twenty-five C associated protein **kinase**) that phosphorylates Cdc25C on **serine** 216 in vitro. C-TAK1 is ubiquitously **expressed** in **human** tissues and cell lines and is distinct from the DNA damage checkpoint **kinase** Chk1, shown previously to phosphorylate Cdc25C on **serine** 216. Cotransfection of Cdc25C with C-TAK1 resulted in enhanced phosphorylation of Cdc25C on **serine** 216. In addition, a physical interaction between C-TAK1 and Cdc25C was observed upon transient overexpression in COS-7 cells. Finally, coproduction of Cdc25C and C-TAK1 in bacteria resulted in the stoichiometric phosphorylation of Cdc25C on **serine** 216 and facilitated 14-3-3 protein binding in vitro. Taken together, these results suggest that one function of C-TAK1 may be to regulate the interactions between Cdc25C and 14-3-3 in vivo by phosphorylating Cdc25C on **serine** 216.

L9 ANSWER 50 OF 63 BIOSIS COPYRIGHT (c) 2005 The Thomson Corporation on STN
ACCESSION NUMBER: 1994:210662 BIOSIS
DOCUMENT NUMBER: PREV199497223662
TITLE: The Histoplasma capsulatum cdc2 gene is transcriptionally regulated during the morphologic transition.
AUTHOR(S): Di Lallo, G.; Gargano, S.; Maresca, B. [Reprint author]
CORPORATE SOURCE: IIGB, Via Marconi 12, 80125 Naples, Italy
SOURCE: Gene (Amsterdam), (1994) Vol. 140, No. 1, pp. 51-57.
CODEN: GENED6. ISSN: 0378-1119.
DOCUMENT TYPE: Article
LANGUAGE: English
OTHER SOURCE: Genbank-X74361
ENTRY DATE: Entered STN: 10 May 1994
Last Updated on STN: 25 Jun 1994

AB To understand the molecular mechanisms that control the reversible morphologic transition from mycelia to yeast in dimorphic fungi, we have isolated and characterized a cdc2 gene from Histoplasma capsulatum. This organism is a dimorphic pathogenic fungus that grows as a filamentous saprobic mold in soil and as a unicellular pathogenic yeast in **human** tissue. The **cloned** gene, whose protein product has a high degree of homology with other members of the cdc2 family, is split into four exons and three introns of 95, 52 and 85 nucleotides. Analyses of cDNA **clones** confirm the presence of the eukaryotic splice donor (GT) and acceptor (AG) sites. The spliced gene codes for a protein of 324 amino acids (aa) with a predicted molecular mass of 36.9 kDa. The H. capsulatum cdc2 product has 71% aa identity with Saccharomyces cerevisiae and 70% with Schizosaccharomyces pombe. The deduced protein contains the sequence, PSTAIRE, that is normally found in most p34-**cdc** proteins. H. capsulatum cdc2 is transcriptionally regulated during the morphologic mycelium-yeast transitions and is more actively transcribed in the yeast than in the mycelial phase.

L9 ANSWER 51 OF 63 BIOSIS COPYRIGHT (c) 2005 The Thomson Corporation on STN
ACCESSION NUMBER: 1991:293102 BIOSIS

DOCUMENT NUMBER: PREV199192014117; BA92:14117
TITLE: IDENTIFICATION OF PHOSPHORYLATED SITES IN THE MOUSE GLUCOCORTICOID RECEPTOR.
AUTHOR(S): BODWELL J E [Reprint author]; ORTI E; COULL J M; PAPPIN D J C; SMITH L I; SWIFT F
CORPORATE SOURCE: DEP PHYSIOL, DARTMOUTH MED SCH, HANOVER, NEW HAMPSHIRE 03756, USA
SOURCE: Journal of Biological Chemistry, (1991) Vol. 266, No. 12, pp. 7549-7555.
CODEN: JBCHA3. ISSN: 0021-9258.
DOCUMENT TYPE: Article
FILE SEGMENT: BA
LANGUAGE: ENGLISH
ENTRY DATE: Entered STN: 25 Jun 1991
Last Updated on STN: 13 Aug 1991

AB Glucocorticoid receptors in vivo are phosphorylated in the absence of hormone and become hyperphosphorylated in the presence of glucocorticoid agonist but not antagonists (Orti, E., Mendel, D. B., Smith, L. I., and Munck, A. (1989) J. Biol. Chemical 264, 9728-9731). As a preliminary step to elucidating the functional significance of receptor phosphorylation, we have identified seven phosphorylated sites at the mouse receptor. Tryptic phosphopeptides from 32P-labeled receptors were purified from glucocorticoid-treated mouse thymoma cells (WEHI-7) and from stably transfected Chinese hamster ovary cells (WCL2) that **express** large numbers of mouse receptors. Phosphopeptide maps of receptors from these two cell types were almost indistinguisable. Solid phase sequencing revealed phosphorylation at **serines** 122, 150, 212, 220, 234, and 315 and **threonine** 159. **Serines** 122, 150, 212, 220, and 234 and the sequences surrounding them are conserved in the homologous regions of the rat and **human** receptors, but **threonine** 159 and **serine** 315 have no homologous in the **human** receptor. The seven phosphorylated sites are in the amino-terminal domain of the receptor. All but **serine** 315 are within transactivation domains identified in the **human** and/or rat receptors. **Serine** 212, 220, and 234 are in a highly acidic region that in the mouse receptor is necessary for full transcription initiation activity and reduces nonspecific DNA binding. **Serines** 212, 220, and 234 and **threonine** 159 are in consensus sequences for proline-directed **kinase** and/or p34cdc2 **kinase**. **Serine** 122 is in a consensus sequence for casein **kinase** II whereas **serines** 150 and 315 do not appear to be in any known **kinase** consensus sequence. The location of many of these sites suggests a role of phosphorylation in transactivation.

L9 ANSWER 52 OF 63 BIOTECHDS COPYRIGHT 2005 THE THOMSON CORP. on STN
ACCESSION NUMBER: 2002-18260 BIOTECHDS
TITLE: New antisense peptides of amyloid beta protein residues 1-32, useful for detecting, preventing and treating Alzheimer's disease, or for identifying therapeutic agents that prevent cytotoxicity or phosphorylation of amyloid beta; vector-mediated **recombinant** protein gene transfer and **expression** in host cell for use in gene therapy, **recombinant** vaccine and nucleic acid vaccine preparation
AUTHOR: MILTON N G N
PATENT ASSIGNEE: INSIGHT BIOTECHNOLOGY LTD
PATENT INFO: WO 2002036614 10 May 2002
APPLICATION INFO: WO 2000-GB4843 1 Nov 2000
PRIORITY INFO: GB 2000-26739 1 Nov 2000
DOCUMENT TYPE: Patent
LANGUAGE: English
OTHER SOURCE: WPI: 2002-490001 [52]
AB DERWENT ABSTRACT:

NOVELTY - A peptide (I) comprising the antisense sequence of amyloid-beta (Abeta) 1-43 consisting of fully defined sequence of 43 amino acids given in the specification, its fragment capable of binding to the Abeta protein within the Abeta 1-43 region, or a homologue of the peptide or fragment having the same hydropathic profile or at least 60% sequence identity, is new.

DETAILED DESCRIPTION - INDEPENDENT CLAIMS are also included for the following: (1) a phosphorylated Abeta protein or its fragment for use in therapy; (2) an isolated **recombinant** vector comprising a polynucleotide encoding (I); (3) an antibody raised against (I); (4) an antibody raised against a protein of (1) having no or reduced affinity for the non-phosphorylated form of the protein; (5) an antibody raised against a peptide comprising a sequence selected from 9 fully defined sequences of 5-29 amino acids (designated p1-p9, respectively) given in the specification; (6) determining if a patient is at risk for Alzheimer's disease by analyzing a sample from the patient that contains Abeta to determine if Abeta is phosphorylated, where phosphorylation indicates a risk of Alzheimer's disease; (7) an assay for identifying an agent that inhibits the interaction of Abeta protein with other protein by contacting Abeta protein or its fragment with a target agent and a peptide that binds to Abeta (or fragment), and determining if the agent inhibits the peptide from binding to Abeta compared to a control assay carried out in the absence of the peptide; (8) an assay for identifying an agent that binds to Abeta within the region Abeta 1-43, by contacting a target agent with a peptide as defined above, and determining if the agent binds to the peptide; (9) a vaccine composition comprising (I), a phosphorylated Abeta protein, or a peptide comprising a sequence selected from p1-p5, and a diluent or adjuvant; and (10) a compound that blocks the activity of a phosphorylated Abeta protein.

BIOTECHNOLOGY - Preferred Peptide: The fragment of the peptide comprises the antisense sequence of Abeta 17-24, Abeta 31-35, Abeta 3-30, Abeta 17-35, Abeta 12-24, Abeta12-28, Abeta 14-35, Abeta 25-35, or their homologue with at least 60% sequence identity. The peptide comprises a sequence selected from 6 fully defined sequences of 43 amino acids given in the specification, or their fragment capable of binding to the Abeta protein within the Abeta 1-43 region. The peptide has a therapeutic or diagnostic agent bound to it, where the diagnostic agent is a detectable label and the therapeutic agent is an inhibitor of a protein **kinase**. The Abeta peptide comprised in the vaccine is phosphorylated on one or more of residues 8, 10, 26 and 43. Preferred Protein: The phosphorylated Abeta protein preferably comprises a phosphorylated **serine** 26 residue. Preferred Method: In determining the risk of a patient to Alzheimer's disease, phosphorylation is detected within the where 1-43 region, specifically the phosphorylation of a **serine** amino acid residue. The sample is treated with an antibody that has affinity for where phosphorylated within the where 1-43 region, and has no reduced affinity for non-phosphorylated Abeta. In the assay for identifying an agent that inhibits interaction of Abeta protein with other protein, the Abeta comprises at least Abeta 1-43, and the peptide is a protein **kinase** enzyme, a cyclin, a catalase ERAB, or their fragments. The protein **kinase** is preferably cdc2. The peptide is less than 40 amino acids in length and comprises a sequence selected from p6-p9. In the assay for identifying an agent that binds to Abeta within the region Abeta 1-43, the peptide is phosphorylated.

ACTIVITY - Nootropic; Neuroprotective.

MECHANISM OF ACTION - Antisense therapy; Vaccine. No supporting data is given in the source material.

USE - (I) is useful in therapy, and in the manufacture of a medicament for therapy of a condition mediated by phosphorylation of Abeta or by binding of endogenous Abeta to catalase, where such condition is Alzheimer's disease. The peptide comprising the amino acid sequence Abeta 1-43 or its fragment capable of binding to cyclin-dependent

kinase is useful in the manufacture of a medicament for therapy of a condition mediated by phosphorylation of Abeta. The protein **kinase** inhibitor may be used in the manufacture of a medicament for treating Alzheimer's disease, where the inhibitor selectively binds to where protein and the **kinase** is p34-cdc22 (all claimed). The antisense peptides may also be used for detecting, preventing and treating Alzheimer's disease, for identifying therapeutic agents that prevent Abeta cytotoxicity or phosphorylation of Abeta, and in vaccines. A phosphorylated Abeta fragment may be used to generate antibodies specific for the phosphorylated form, or as an antigen in a vaccine composition.

EXAMPLE - The forward amyloid beta (Abeta) antisense peptide (AbetaAS(F)) 1-43 (consisting of 43 amino acids) was derived by reading the complementary (non-coding) strand of DNA from the region encoding the Abeta 1-43 peptide in the 3'-5' direction, where the DNA encoded a stop codon, the nearest suitable replacement amino acid was substituted. The AbetaAS(F) sequence was used in basic local alignment search tool (BLAST) search to identify proteins with sequence similarity. Results showed a region of sequence similarity with the AbetaAS(F) 3-30 sequence having 46% identity and 68% similarity with the **human** cdc2 105-132 region (consisting of 28 amino acids). This indicated that Abeta 1-43 may be phosphorylated **cdc**-2. BLAST comparison between AbetaAS and **human** cdc2 (accession number GI 87058) also identified 3 other regions of sequence similarity. Cdc2 residues 56-63 (Lys-Glu-Leu-Arg-His-Pro-Asn-Ile) showing 50% identity and 75% similarity with AbetaAS 20-27; cdc2 residues 95-99 (Pro-Pro-Gly-Gln-Tyr) showing 80% identity with AbetaAS 37-41; and cdc2 residues 229-238 (Pro-Glu-Val-Glu-Ser-Leu-Gln-Asp-Tyr-Lys) showing 40% identity and 50% similarity with AbetaAS 33-42. (44 pages)

L9 ANSWER 53 OF 63 SCISEARCH COPYRIGHT (c) 2005 The Thomson Corporation on STN

ACCESSION NUMBER: 1991:466793 SCISEARCH
THE GENUINE ARTICLE: GB448
TITLE: A NEW **HUMAN** P34 PROTEIN-**KINASE**, CDK2, IDENTIFIED BY COMPLEMENTATION OF A CDC28 MUTATION IN SACCHAROMYCES-CEREVISIAE, IS A HOMOLOG OF XENOPUS-EG1
AUTHOR: ELLEDGE S J (Reprint); SPOTTSWOOD M R
CORPORATE SOURCE: BAYLOR COLL MED, DEPT BIOCHEM, HOUSTON, TX 77030 (Reprint); BAYLOR COLL MED, INST MOLEC GENET, HOUSTON, TX 77030
COUNTRY OF AUTHOR: USA
SOURCE: EMBO JOURNAL, (SEP 1991) Vol. 10, No. 9, pp. 2653-2659. ISSN: 0261-4189.
PUBLISHER: OXFORD UNIV PRESS UNITED KINGDOM, WALTON ST JOURNALS DEPT, OXFORD, ENGLAND OX2 6DP.
DOCUMENT TYPE: Article; Journal
FILE SEGMENT: LIFE
LANGUAGE: English
REFERENCE COUNT: 40
ENTRY DATE: Entered STN: 1994
Last Updated on STN: 1994
ABSTRACT IS AVAILABLE IN THE ALL AND IALL FORMATS

AB The onset of S-phase and M-phase in both Schizosaccharomyces pombe and Saccharomyces cerevisiae requires the function of the cdc2/CDC28 gene product, p34, a **serine-threonine** protein **kinase**. A **human** homolog, p34cdc2, was identified by functional complementation of the S. pombe cdc2 mutation (Lee and Nurse, 1987). Using a **human** cDNA **expression** library to search for suppressors of cdc28 mutations in S. cerevisiae, we have identified a second functional p34 homolog, CDK2 cell division **kinase**). This gene is **expressed** as a 2.1 kb transcript encoding a polypeptide of 298 amino acids. This protein retains nearly

all of the amino acids highly conserved among previously identified p34 homologs from other species, but is considerably divergent from all previous p34cdc2 homologs, approximately 65% identity. This gene encodes the **human** homolog of the Xenopus Eg1 gene, sharing 89% amino acid identity, and defines a second sub-family of CDC2 homologs. A second chromosomal mutation which arose spontaneously was required to allow complementation of the cdc28-4 mutation by CDK2. This mutation blocked the ability of this strain to mate. These results suggest that the machinery controlling the **human** cell cycle is more complex than that for fission and budding yeast.

L9 ANSWER 54 OF 63 HCAPLUS COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER: 2005:523313 HCAPLUS
DOCUMENT NUMBER: 143:38415
TITLE: Biomarkers for the efficacy of calcitonin and parathyroid hormone analog treatment
INVENTOR(S): Bobadilla, Maria
PATENT ASSIGNEE(S): Novartis A.-G., Switz.; Novartis Pharma G.m.b.H.
SOURCE: PCT Int. Appl., 89 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2005053731	A1	20050616	WO 2004-EP13347	20041124

W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NA, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW
RW: BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IS, IT, LU, MC, NL, PL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG

PRIORITY APPLN. INFO.: US 2003-525025P P 20031125
AB Gene **expression** assays were performed using tissues of monkeys treated with the calcitonin or parathyroid hormone analog (e.g., PTS 893) at sub-therapeutic dose. The assays were analyzed to identify the modes of actions of calcitonin or parathyroid hormone with relationships to therapeutic applications. Among the biomarkers are the **expression** profiles of the genes for Y-box binding protein, bone morphogenetic proteins, fibroblast growth factors, insulin-like growth factors, vascular endothelial growth factor, α-2-HS glycoprotein, osteoclast stimulating factor, nuclear receptors (steroid/thyroid family), and others. The results obtained support the anabolic effect of salmon calcitonin on bone metabolism
REFERENCE COUNT: 4 THERE ARE 4 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L9 ANSWER 55 OF 63 HCAPLUS COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER: 2005:447673 HCAPLUS
DOCUMENT NUMBER: 143:20875
TITLE: Differentially **expressed** gene profile for diagnosing and treating mental disorders
INVENTOR(S): Akil, Huda; Atz, Mary; Bunney, William E., Jr.; Choudary, Prabhakara V.; Evans, Simon J.; Jones, Edward G.; Li, Jun; Lopez, Juan F.; Myers, Richard; Thompson, Robert C.; Tomita, Hiroaki; Vawter, Marquis

P.; Watson, Stanley
PATENT ASSIGNEE(S): The Board of Trustees of the Leland Stanford Junior University, USA
SOURCE: PCT Int. Appl., 226 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2005046434	A2	20050526	WO 2004-US36784	20041105

W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NA, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW
RW: BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IS, IT, LU, MC, NL, PL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG

PRIORITY APPLN. INFO.: US 2003-517751P P 20031105
US 2004-982556 A 20041104

AB The present invention provides methods for diagnosing mental disorders (e.g., psychotic disorders such as schizophrenia). The present invention uses DNA microarray anal. to demonstrate differential **expression** of genes in selected regions of post-mortem brains from patients diagnosed with mental disorders in comparison with normal control subjects. The invention also provides methods of identifying modulators of such mental disorders as well as methods of using these modulators to treat patients suffering from such mental disorders.

L9 ANSWER 56 OF 63 HCAPLUS COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER: 2005:409663 HCAPLUS
DOCUMENT NUMBER: 142:461604
TITLE: Genes showing altered levels of **expression** in blood for use as markers for the early diagnosis of liver cancer
INVENTOR(S): Liew, Choong-chin; Yager, Tom; Dempsey, Adam; Chao, Manuel
PATENT ASSIGNEE(S): Genenews, Inc., Can.; Williams, Kathleen M.
SOURCE: PCT Int. Appl., 278 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2005042725	A2	20050512	WO 2004-US36603	20041103

W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NA, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW
RW: BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IS, IT, LU, MC, NL, PL, PT, RO,

SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG

US 2005152908 A1 20050714 US 2004-980850 20041103
PRIORITY APPLN. INFO.: US 2003-516853P P 20031103

AB Genes that show altered levels of **expression** the blood and that can be used as early indicators in the diagnosis of liver cancer are identified. The invention further relates to useful combinations of these markers for diagnosing liver cancer. The invention further provides for the polynucleotides and polypeptides and kits thereof for use as a tool to diagnose disease and to monitor the efficacy of therapeutic regimens. The invention further provides a method of selecting biomarker combinations and the combinations thus identified for diagnosis of liver cancer. Also encompassed by the invention are screening methods to identify therapeutic targets for treating liver cancer, and identify single nucleotide point mutations related to liver cancer. Identification of genes showing altered levels of **expression** in liver cancer by blood anal. and correlation anal. is demonstrated.

L9 ANSWER 57 OF 63 HCAPLUS COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER: 2004:847638 HCAPLUS
DOCUMENT NUMBER: 141:325696
TITLE: Genes showing altered levels of **expression** in response to inhibitors of cyclin-dependent **kinases** and their use in screening for novel inhibitors
INVENTOR(S): Green, Simon R.; Frame, Sheelagh; Blake, David
PATENT ASSIGNEE(S): Cyclacel Limited, UK
SOURCE: PCT Int. Appl., 175 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2004087954	A2	20041014	WO 2004-GB1334	20040326
WO 2004087954	A3	20050127		

W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NA, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW
RW: BW, GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG

PRIORITY APPLN. INFO.: GB 2003-7643 A 20030402

AB Genes that show changes in levels of **expression** in response to pharmaceutical inhibitors of cyclin-dependent **kinases**, especially 2,6,9-tri-substituted purines including roscovitine, are identified for use in the screening for roscovitine-like drugs using either animals or cultured cells. The identity of these markers facilitates the convenient identification of roscovitine-like activity both in vitro and in vivo.

L9 ANSWER 58 OF 63 HCAPLUS COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER: 2004:371153 HCAPLUS
DOCUMENT NUMBER: 140:371494
TITLE: Binary prediction tree modeling with many predictors and its uses in clinical and genomic applications
INVENTOR(S): Nevins, Joseph R.; West, Mike; Huang, Andrew T.

PATENT ASSIGNEE(S): Duke University, USA
SOURCE: PCT Int. Appl., 886 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 5
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2004038376	A2	20040506	WO 2003-US33946	20031024
WO 2004038376	A3	20040826		

W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW

RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG

WO 2004038376	A2	20040506	WO 2003-XA33946	20031024

W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW, AM, AZ, BY, KG, KZ, MD

RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG

WO 2004038376	A2	20040506	WO 2003-XB33946	20031024

W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW, AM, AZ, BY, KG, KZ, MD

RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG

PRIORITY APPLN. INFO.:		
US 2002-420729P	P	20021024
US 2002-421062P	P	20021025
US 2002-421102P	P	20021025
US 2002-424701P	P	20021108
US 2002-424715P	P	20021108
US 2002-424718P	P	20021108
US 2002-425256P	P	20021112
US 2003-448461P	P	20030221
US 2003-448462P	P	20030221
US 2003-457877P	P	20030327
US 2003-458373P	P	20030331
WO 2003-US33946	A	20031024

AB The statistical anal. described and claimed is a predictive statistical tree model that overcomes several problems observed in prior statistical models and regression analyses, while ensuring greater accuracy and predictive capabilities. Although the claimed use of the predictive statistical tree model described herein is directed to the prediction of a

disease in individuals, the claimed model can be used for a variety of applications including the prediction of disease states, susceptibility of disease states or any other biol. state of interest, as well as other applicable non-biol. states of interest. This model first screens genes to reduce noise, applies kmeans correlation-based clustering targeting a large number of clusters, and then uses singular value decompns. (SVD) to extract the single dominant factor (principal component) from each cluster. This generates a statistically significant number of cluster-derived singular factors, that are referred to as metagenes, that characterize multiple patterns of **expression** of the genes across samples. The strategy aims to extract multiple such patterns while reducing dimension and smoothing out gene-specific noise through the aggregation within clusters. Formal predictive anal. then uses these metagenes in a Bayesian classification tree anal. This generates multiple recursive partitions of the sample into subgroups (the 'leaves' of the classification tree), and assocs. Bayesian predictive probabilities of outcomes with each subgroup. Overall predictions for an individual sample are then generated by averaging predictions, with appropriate wts., across many such tree models. The model includes the use of iterative out-of-sample, cross-validation predictions leaving each sample out of the data set one at a time, refitting the model from the remaining samples and using it to predict the hold-out case. This rigorously tests the predictive value of a model and mirrors the real-world prognostic context where prediction of new cases as they arise is the major goal.

L9 ANSWER 59 OF 63 HCAPLUS COPYRIGHT 2005 ACS on STN

ACCESSION NUMBER: 2004:127023 HCAPLUS
DOCUMENT NUMBER: 140:332711
TITLE: Effect of **human** chorionic gonadotropin in the gene **expression** profile of MCF-7 cells
AUTHOR(S): Guo, Shanchun; Russo, Irma H.; Lareef, M. Hasan; Russo, Jose
CORPORATE SOURCE: Breast Cancer Research Laboratory, Fox Chase Cancer Center, Philadelphia, PA, 19111, USA
SOURCE: International Journal of Oncology (2004), 24(2), 399-407
CODEN: IJONES; ISSN: 1019-6439
PUBLISHER: International Journal of Oncology
DOCUMENT TYPE: Journal
LANGUAGE: English

AB The preventive effect of **human** chorionic gonadotropin (hCG)-induced differentiation on exptl. mammary carcinogenesis has been reported to be due to the inhibition of cell proliferation, increased DNA repair capabilities of the mammary epithelium, decreased binding of the carcinogen to the DNA and activation of programmed cell death genes leading to apoptosis. To further our understanding of the mol. pathway of the hCG action on mammary epithelial cells we have analyzed gene **expression** profiles of MCF-7 cells treated with hCG for 24, 48, and 96 h, using a DNA microarray consisting of 1176 genes. Comparison of **expression** between the treated and not treated cells enabled us to identify 48 genes that are affected by this hormone. Importantly, there is a cluster of genes that are overexpressed during the first 24 h and level off thereafter, whereas other genes are maximally **expressed** at 96 h of treatment. The results obtained in this study demonstrated that genes regulating cell proliferation, apoptosis, cell trafficking, and DNA repair are significantly affected by hCG in **human** breast cancer cells in vitro.

REFERENCE COUNT: 113 THERE ARE 113 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L9 ANSWER 60 OF 63 HCAPLUS COPYRIGHT 2005 ACS on STN

ACCESSION NUMBER: 2003:377088 HCAPLUS
DOCUMENT NUMBER: 138:380384
TITLE: Method and device for detecting and monitoring alcoholism and related diseases using microarrays
INVENTOR(S): Harris, Adron; Mayfield, Dayne R.; Lewohl, Jo; Dodd, Peter R.
PATENT ASSIGNEE(S): University of Texas System, USA
SOURCE: PCT Int. Appl., 48 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2003040414	A1	20030515	WO 2002-US35902	20021108
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, OM, PH, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TN, TR, TT, TZ, UA, UG, UZ, VN, YU, ZA, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG				
US 2003104457	A1	20030605	US 2002-291247	20021107
EP 1451374	A1	20040901	EP 2002-802883	20021108
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR, BG, CZ, EE, SK				
JP 2005508199	T2	20050331	JP 2003-542659	20021108
PRIORITY APPLN. INFO.:			US 2001-338270P P	20011108
			WO 2002-US35902 W	20021108

AB A device and method for detecting, diagnosing, and or monitoring alcoholism and related disease states is disclosed. The device includes a substrate and one or more alcoholism-specific nucleic acids attached to the substrate. The substrate is contacted by a sample collected from a person with alcoholism or alc. abuse or an alc. related disease state, wherein contact occurs under pre-selected binding conditions that provides information that can be collected and recorded by a computer.
REFERENCE COUNT: 4 THERE ARE 4 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L9 ANSWER 61 OF 63 HCAPLUS COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER: 2003:356640 HCAPLUS
DOCUMENT NUMBER: 138:380471
TITLE: Genes that are differentially **expressed** during erythropoiesis and their diagnostic and therapeutic uses
INVENTOR(S): Brissette, William H.; Neote, Kuldeep S.; Zagouras, Panayiotis; Zenke, Martin; Lemke, Britt; Hacker, Christine
PATENT ASSIGNEE(S): Pfizer Products Inc., USA; Max-Delbrueck-Centrum Fuer Molekulare Medizin
SOURCE: PCT Int. Appl., 285 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 2
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE

WO 2003038130	A2	20030508	WO 2002-US34888	20021031
WO 2003038130	A3	20040212		
WO 2003038130	C1	20040422		

W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, OM, PH, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZM, ZW

RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG

CA 2460283	AA	20030508	CA 2002-2460283	20021031
WO 2003038130	A2	20030508	WO 2002-XA34888	20021031

W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, OM, PH, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM

RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG

US 2004014064	A1	20040122	US 2002-285366	20021031
EP 1446507	A2	20040818	EP 2002-798424	20021031

R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR, BG, CZ, EE, SK

PRIORITY APPLN. INFO.:	US 2001-335048P	P 20011031
	US 2001-335183P	P 20011102
	WO 2002-US34888	W 20021031

AB The present invention provides mol. targets that regulate erythropoiesis. Groups of genes or their encoded gene products comprise panels of the invention and may be used in therapeutic intervention, therapeutic agent screening, and in diagnostic methods for diseases and/or disorders of erythropoiesis. The panels were discovered using gene **expression** profiling of erythroid progenitors with Affymetrix HU6800 and HG-U95Av2 chips. Cells from an in vitro growth and differentiation system of SCF-Epo dependent **human** erythroid progenitors, E-cadherin+/CD36+ progenitors, cord blood, or CD34+ peripheral blood stem cells were analyzed. The HU6800 chip contains probes from 13,000 genes with a potential role in cell growth, proliferation, and differentiation and the HG-U95Av2 chip contains 12,000 full-length, functionally-characterized genes. This abstract record is one of two records for this document necessitated by the large number of index entries required to fully index the document and publication system constraints.

L9 ANSWER 62 OF 63 HCAPLUS COPYRIGHT 2005 ACS on STN

ACCESSION NUMBER:	1995:446217 HCAPLUS
DOCUMENT NUMBER:	123:104069
TITLE:	**Cloning** of a full-length cDNA sequence encoding A **cdc**-2-related protein **kinase** from **human** endothelial cells
AUTHOR(S):	Best, Jennifer L.; Presky, David H.; Swerlick, Robert A.; Burns, Daniel K.; Chu, Wei
CORPORATE SOURCE:	Department of Inflammation/Autoimmune Diseases, Hoffmann-La Roche Inc., Nutley, NJ, 07110, USA
SOURCE:	Biochemical and Biophysical Research Communications (1995), 208(2), 562-8

CODEN: BBRCA9; ISSN: 0006-291X
PUBLISHER: Academic
DOCUMENT TYPE: Journal
LANGUAGE: English
AB CDNA **clones** encoding a novel **serine/threonine** protein **kinase** were isolated from **human** endothelial cell cDNA libraries. The compiled nucleotide sequence is 1757 base pairs in length and contains an open reading frame encoding a 372 amino acid protein, designated C-2k, with a calculated mol. weight of 43 kDa. Sequence anal. indicates that C-2k contains a conserved protein **kinase** catalytic domain of 308 residues which exhibits its highest sequence identity of 42% to members of the cdc2 **kinase** family and contains the structural elements characteristic to cdc2-like **kinases**. C-2k may therefore represent a new member of the cdc2 **kinase** family.

L9 ANSWER 63 OF 63 LIFESCI COPYRIGHT 2005 CSA on STN
ACCESSION NUMBER: 2004:82818 LIFESCI
TITLE: The evolving roles of alternative splicing
AUTHOR: Lareau, L.F.; Green, R.E.; Bhatnagar, R.S.; Brenner, S.E.
CORPORATE SOURCE: Departments of Molecular and Cell Biology, University of California, Berkeley, California 94720, USA; E-mail: brenner@compbio.berkeley.edu
SOURCE: Current Opinion in Structural Biology [Curr. Opin. Struct. Biol.], (20040600) vol. 14, no. 3, pp. 273-282. ISSN: 0959-440X.
DOCUMENT TYPE: Journal
TREATMENT CODE: General Review
FILE SEGMENT: N
LANGUAGE: English
SUMMARY LANGUAGE: English
AB Alternative splicing is now commonly thought to affect more than half of all **human** genes. Recent studies have investigated not only the scope but also the biological impact of alternative splicing on a large scale, revealing that its role in generating proteome diversity may be augmented by a role in regulation. For instance, protein function can be regulated by the removal of interaction or localization domains by alternative splicing. Alternative splicing can also regulate gene **expression** by splicing transcripts into unproductive mRNAs targeted for degradation. To fully understand the scope of alternative splicing, we must also determine how many of the predicted splice variants represent functional forms. Comparisons of alternative splicing between **human** and mouse genes show that predominant splice variants are usually conserved, but rare variants are less commonly shared. Evolutionary conservation of splicing patterns suggests functional importance and provides insight into the evolutionary history of alternative splicing. Clk, **CDC**-like **kinase**; EST, **expressed** sequence tag; FGF, fibroblast growth factor; FGFR, fibroblast growth factor receptor; NMD, nonsense-mediated mRNA decay; PTB, polypyrimidine tract binding protein; PTC, premature termination codon; RUST, regulated unproductive splicing and translation; SR, **serine** /arginine-rich; TMV, tobacco mosaic virus; TNFR, tumor necrosis factor receptor; UTR, untranslated region

=> d his

(FILE 'HOME' ENTERED AT 12:23:37 ON 28 JUL 2005)

FILE 'MEDLINE, EMBASE, BIOSIS, BIOTECHDS, SCISEARCH, HCAPLUS, NTIS, LIFESCI' ENTERED AT 12:24:27 ON 28 JUL 2005
L1 1340563 S KINASE?
L2 441287 S SERINE OR THREONINE

```
L3       111458 S L1 AND L2
L4        30908 S "CDC"
L5          285 S L3 AND L4
L6      7187685 S CLON? OR EXPRESS? OR RECOMBINANT
L7          142 S L5 AND L6
L8          112 DUP REM L7 (30 DUPLICATES REMOVED)
L9           63 S HUMAN AND L8

=> s "serine and arginine rich"
   2 FILES SEARCHED...
   5 FILES SEARCHED...
L10         126 "SERINE AND ARGININE RICH"

=> s l9 and l10
L11           1 L9 AND L10

=> d all

L11 ANSWER 1 OF 1  LIFESCI    COPYRIGHT 2005 CSA on STN
AN   2004:82818  LIFESCI
TI   The evolving roles of alternative splicing
AU   Lareau, L.F.; Green, R.E.; Bhatnagar, R.S.; Brenner, S.E.
CS   Departments of Molecular and Cell Biology, University of California,
     Berkeley, California 94720, USA; E-mail: brenner@compbio.berkeley.edu
SO   Current Opinion in Structural Biology [Curr. Opin. Struct. Biol.],
     (20040600) vol. 14, no. 3, pp. 273-282.
     ISSN: 0959-440X.
DT   Journal
TC   General Review
FS   N
LA   English
SL   English
AB   Alternative splicing is now commonly thought to affect more than half of
     all human genes. Recent studies have investigated not only the
     scope but also the biological impact of alternative splicing on a large
     scale, revealing that its role in generating proteome diversity may be
     augmented by a role in regulation. For instance, protein function can be
     regulated by the removal of interaction or localization domains by
     alternative splicing. Alternative splicing can also regulate gene
     expression by splicing transcripts into unproductive mRNAs
     targeted for degradation. To fully understand the scope of alternative
     splicing, we must also determine how many of the predicted splice variants
     represent functional forms. Comparisons of alternative splicing between
     human and mouse genes show that predominant splice variants are
     usually conserved, but rare variants are less commonly shared.
     Evolutionary conservation of splicing patterns suggests functional
     importance and provides insight into the evolutionary history of
     alternative splicing. Clk, CDC-like kinase; EST,
     expressed sequence tag; FGF, fibroblast growth factor; FGFR,
     fibroblast growth factor receptor; NMD, nonsense-mediated mRNA decay; PTB,
     polypyrimidine tract binding protein; PTC, premature termination codon;
     RUST, regulated unproductive splicing and translation; SR, serine
     /arginine-rich; TMV, tobacco mosaic virus; TNFR, tumor
     necrosis factor receptor; UTR, untranslated region
CC   14100 Reviews
UT   Reviews; Splicing; Evolution; man; mice


=> d his

     (FILE 'HOME' ENTERED AT 12:23:37 ON 28 JUL 2005)

     FILE 'MEDLINE, EMBASE, BIOSIS, BIOTECHDS, SCISEARCH, HCAPLUS, NTIS,
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     LIFESCI' ENTERED AT 12:24:27 ON 28 JUL 2005
L1       1340563 S KINASE?
L2        441287 S SERINE OR THREONINE
L3        111458 S L1 AND L2
L4         30908 S "CDC"
L5           285 S L3 AND L4
L6       7187685 S CLON? OR EXPRESS? OR RECOMBINANT
L7           142 S L5 AND L6
L8           112 DUP REM L7 (30 DUPLICATES REMOVED)
L9            63 S HUMAN AND L8
L10          126 S "SERINE AND ARGININE RICH"
L11            1 S L9 AND L10

=> s "clk4"
L12           58 "CLK4"

=> s l6 and l12
L13           48 L6 AND L12

=> dup rem l13
PROCESSING COMPLETED FOR L13
L14           21 DUP REM L13 (27 DUPLICATES REMOVED)

=> d 1-21 ibib ab

L14  ANSWER 1 OF 21  HCAPLUS  COPYRIGHT 2005 ACS on STN DUPLICATE 1
ACCESSION NUMBER:         2005:156228  HCAPLUS
                            Correction of: 2005:16967
DOCUMENT NUMBER:          142:192331
                            Correction of: 142:108390
TITLE:                    Quantitative RT-PCR method for the detection in blood
                          of microarray-identified rheumatoid arthritis-related
                          gene transcripts for diagnosing and monitoring disease
                          state
INVENTOR(S):              Liew, Choong-Chin
PATENT ASSIGNEE(S):       Chondrogene Limited, Can.
SOURCE:                   U.S. Pat. Appl. Publ., 81 pp., Cont.-in-part of U.S.
                          Ser. No. 802,875.
                          CODEN: USXXCO
DOCUMENT TYPE:            Patent
LANGUAGE:                 English
FAMILY ACC. NUM. COUNT:   46
PATENT INFORMATION:

     PATENT NO.           KIND   DATE        APPLICATION NO.          DATE
     ---------------      ----   --------    ---------------------    --------
     US 2005003394         A1    20050106    US 2004-812782           20040330
     US 2004014059         A1    20040122    US 2002-268730           20021009
     US 2004265869         A1    20041230    US 2004-812716           20040330
     US 2005003394         A1    20050106    US 2004-812782           20040330
     US 2005003394         A1    20050106    US 2004-812782           20040330
PRIORITY APPLN. INFO.:                       US 1999-115125P      P   19990106
                                             US 2000-477148       B1  20000104
                                             US 2002-268730       A2  20021009
                                             US 2003-601518       A2  20030620
                                             US 2004-802875       A2  20040312
                                             US 2004-812782       A   20040330
AB   The present invention is directed to detection and measurement of gene
     transcripts and their equivalent nucleic acid products in blood for
diagnosing
     and monitoring diseases.  The present invention demonstrates that a simple
     drop of blood may be used to determine the quant. expression of
     various mRNAs that reflect the health/disease state of the subject through
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the use of quant. reverse transcription-polymerase chain reaction (QRT-PCR) anal. Specifically provided is anal. performed on a drop of blood for detecting, diagnosing and monitoring rheumatoid arthritis using gene-specific and/or tissue-specific primers. The present invention also describes methods by which delineation of the sequence and/or quantitation of the **expression** levels of disease-specific genes allows for an immediate and accurate diagnostic/prognostic test for disease or to assess the effect of a particular treatment regimen.

L14 ANSWER 2 OF 21 HCAPLUS COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER: 2005:76353 HCAPLUS
DOCUMENT NUMBER: 142:171035
TITLE: Diagnosis of non-central nervous system (CNS) diseases by analysis of changes in patterns of gene **expression** in the central nervous system
INVENTOR(S): Podhajcer, Osvaldo L.; Pitossi, Fernando Juan; Rubinstein, Marcelo
PATENT ASSIGNEE(S): Gentron, LLC, USA
SOURCE: PCT Int. Appl., 302 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2005007892	A1	20050127	WO 2004-US21543	20040702

W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NA, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW
RW: BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG

PRIORITY APPLN. INFO.: US 2003-484683P P 20030703
US 2003-484726P P 20030703

AB The invention features methods, systems, and compns. for diagnosing noncentral nervous system (non-CNS) disorders by detecting changes in gene **expression** in the CNS, e.g., in cerebrospinal fluid, in brain or spinal cord tissue samples, or other bodily fluid samples. Methods of diagnosis of diseases that do not originate in the central nervous system (CNS) by measuring their effects on patterns of gene **expression** in the central nervous system are described. The method may be used on samples including cerebrospinal fluid, in brain or spinal cord tissue samples, or other body fluids.

REFERENCE COUNT: 9 THERE ARE 9 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L14 ANSWER 3 OF 21 HCAPLUS COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER: 2005:607197 HCAPLUS
TITLE: Gene **expression** profiling for diagnosis, prognosis, and therapy of osteoarthritis and other diseases using microarrays
INVENTOR(S): Liew, Choong-Chin
PATENT ASSIGNEE(S): Chondrogene Limited, Can.
SOURCE: U.S. Pat. Appl. Publ., 157 pp., Cont.-in-part of U.S. Ser. No. 802,875.
CODEN: USXXCO

DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 46
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.		DATE
US 2005123938	A1	20050609	US 2004-809675		20040325
US 2004037841	A1	20040226	US 2002-85783		20020228
US 2004014059	A1	20040122	US 2002-268730		20021009
US 2005123938	A1	20050609	US 2004-809675		20040325
PRIORITY APPLN. INFO.:			US 1999-115125P	P	19990106
			US 2000-477148	B1	20000104
			US 2001-271955P	P	20010228
			US 2001-275017P	P	20010312
			US 2001-305340P	P	20010713
			US 2002-85783	A2	20020228
			US 2002-268730	A2	20021009
			US 2003-601518	A2	20030620
			US 2004-802875	A2	20040312
			US 2004-809675	A	20040325

AB The present invention relates to gene **expression** profiling for diagnosis, prognosis and therapy of osteoarthritis and other diseases using microarray methods. Specifically provided is anal. performed on a drop of blood for detecting, diagnosing and monitoring diseases using gene-specific and/or tissue-specific primers. Affymetrix Human Genome U133 and ChondroChip microarrays were used todetect differentially **expressed** gene transcripts in hypertension, obesity, allergy, systemic steroids, coronary artery disease, diabetes type 2, hyperlipidemia, lung disease, bladder cancer, rheumatoid arthritis, osteoarthritis, liver cancer, schizophrenia, Chagas disease, asthma, and manic depression syndrome. The present invention also describes methods by which delineation of the sequence and/or quantitation of the **expression** levels of disease-specific genes allows for an immediate and accurate diagnostic/prognostic test for disease or to assess the effect of a particular treatment regimen. [This abstract record is one of 3 records for this document necessitated by the large number of index entries required to fully index the document and publication system constraints.].

L14 ANSWER 4 OF 21 HCAPLUS COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER: 2005:172212 HCAPLUS
DOCUMENT NUMBER: 142:259425
TITLE: Gene **expression** profiles and biomarkers for the detection of asthma-related and other disease-related gene transcripts in blood
INVENTOR(S): Liew, Choong-Chin
PATENT ASSIGNEE(S): Chondrogene Limited, Can.
SOURCE: U.S. Pat. Appl. Publ., 156 pp., Cont.-in-part of U.S. Ser. No. 802,875.
CODEN: USXXCO
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 46
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.		DATE
US 2005042630	A1	20050224	US 2004-816357		20040401
US 2004014059	A1	20040122	US 2002-268730		20021009
US 2005042630	A1	20050224	US 2004-816357		20040401
PRIORITY APPLN. INFO.:			US 1999-115125P	P	19990106
			US 2000-477148	B1	20000104

	US 2002-268730	A2 20021009
	US 2003-601518	A2 20030620
	US 2004-802875	A2 20040312
	US 2004-816357	A 20040401

AB The present invention is directed to detection and measurement of gene transcripts and their equivalent nucleic acid products in blood. Specifically provided is anal. performed on a drop of blood for detecting, diagnosing, and monitoring diseases, and in particular asthma, using gene-specific and/or tissue-specific primers. Affymetrix Human Genome U133 and ChondroChip microarrays were used to detect differentially **expressed** gene transcripts in hypertension, obesity, allergy, systemic steroids, coronary artery disease, diabetes type 2, hyperlipidemia, lung disease, bladder cancer, rheumatoid arthritis, osteoarthritis, liver cancer, schizophrenia, Chagas disease, asthma, and manic depression syndrome. The present invention describes methods by which delineation of the sequence and/or quantitation of the **expression** levels of disease-specific genes allows for an immediate and accurate diagnostic/prognostic test for disease or to assess the effect of a particular treatment regimen. [This abstract record is one of three records for this document necessitated by the large number of index entries required to fully index the docoment and publication system constraints.].

L14 ANSWER 5 OF 21 HCAPLUS COPYRIGHT 2005 ACS on STN DUPLICATE 2

ACCESSION NUMBER:	2005:156681 HCAPLUS Correction of: 2005:60757
DOCUMENT NUMBER:	142:216629 Correction of: 142:132329
TITLE:	Gene **expression** profiles and biomarkers for the detection of hyperlipidemia and other disease-related gene transcripts in blood
INVENTOR(S):	Liew, Choong-Chin
PATENT ASSIGNEE(S):	Chondrogene Limited, Can.
SOURCE:	U.S. Pat. Appl. Publ., 155 pp., Cont.-in-part of U.S. Ser. No. 802,875. CODEN: USXXCO
DOCUMENT TYPE:	Patent
LANGUAGE:	English
FAMILY ACC. NUM. COUNT:	46

PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
US 2004248170	A1	20041209	US 2004-812777	20040330
US 2004014059	A1	20040122	US 2002-268730	20021009
US 2004248170	A1	20041209	US 2004-812777	20040330
US 2004248170	A1	20041209	US 2004-812777	20040330
US 2004265869	A1	20041230	US 2004-812716	20040330

PRIORITY APPLN. INFO.:	US 1999-115125P	P 19990106
	US 2000-477148	B1 20000104
	US 2002-268730	A2 20021009
	US 2003-601518	A2 20030620
	US 2004-802875	A2 20040312
	US 2004-812777	A 20040330

AB The present invention is directed to detection and measurement of gene transcripts and their equivalent nucleic acid products in blood. Specifically provided is anal. performed on a drop of blood for detecting, diagnosing, and monitoring diseases, and in particular hyperlipidemia, using gene-specific and/or tissue-specific primers. Affymetrix Human Genome U133 and ChondroChip microarrays were used to detect differentially **expressed** gene transcripts in hypertension, obesity, allergy,

systemic steroids, coronary artery disease, diabetes type 2, hyperlipidemia, lung disease, bladder cancer, rheumatoid arthritis, osteoarthritis, liver cancer, schizophrenia, Chagas disease, asthma, and manic depression syndrome. The present invention describes methods by which delineation of the sequence and/or quantitation of the **expression** levels of disease-specific genes allows for an immediate and accurate diagnostic/prognostic test for disease or to assess the effect of a particular treatment regimen.

L14 ANSWER 6 OF 21 HCAPLUS COPYRIGHT 2005 ACS on STN DUPLICATE 3
ACCESSION NUMBER: 2004:204306 HCAPLUS
DOCUMENT NUMBER: 140:234408
TITLE: Differentially **expressed** nucleic acids in human leukocytes useful for diagnosing or monitoring autoimmune and chronic inflammatory diseases
INVENTOR(S): Wohlgemuth, Jay; Fry, Kirk; Woodward, Robert; Ly, Ngoc
PATENT ASSIGNEE(S): USA
SOURCE: U.S. Pat. Appl. Publ., 484 pp., Cont.-in-part of U.S. Ser. No. 6,290.
CODEN: USXXCO
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 9
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
US 2004009479	A1	20040115	US 2002-131827	20020424
US 2004009479	A1	20040115	US 2002-131827	20020424
US 6905827	B2	20050614		

PRIORITY APPLN. INFO.: US 2001-296764P P 20010608
US 2001-6290 A2 20011022
US 2002-131827 A 20020424

AB Methods of diagnosing or monitoring an autoimmune or chronic inflammatory disease, particularly systemic lupus erythematosis (SLE) in a patient by detecting the **expression** level of one or more genes or surrogates derived therefrom in the patient are described. Diagnostic oligonucleotides for diagnosing or monitoring chronic inflammatory disease, particularly SLE infection and kits or systems containing the same are also described. Thus, over 8000 50-mer oligonucleotide microarray probes are designed from human leukocyte, plant, and viral genes identified by subtractive hybridization, sequencing, and database mining as candidates for human clin. conditions. Six hundred twenty-three cDNA sequences derived from human leukocytes were not homologous to UniGene sequences or sequences found in dbEST at the time they were search. The invention also provides lupus gene **expression** markers, PCR primers for each of the lupus markers, and surrogates for the lupus gene **expression** markers. [This abstract record is one of several records for this document necessitated by the large number of index entries required to fully index the document and publication system constraints.].

L14 ANSWER 7 OF 21 HCAPLUS COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER: 2005:112752 HCAPLUS
DOCUMENT NUMBER: 142:153475
TITLE: Gene **expression** profiles and biomarkers for the detection of depression-related and other disease-related gene transcripts in blood
INVENTOR(S): Liew, Choong-Chin
PATENT ASSIGNEE(S): Chondrogene Limited, Can.
SOURCE: U.S. Pat. Appl. Publ., 154 pp., Cont.-in-part of U.S. Ser. No. 802,875.
CODEN: USXXCO
DOCUMENT TYPE: Patent

LANGUAGE: English
FAMILY ACC. NUM. COUNT: 46
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
US 2004265868	A1	20041230	US 2004-812702	20040330
US 2004014059	A1	20040122	US 2002-268730	20021009
US 2004265868	A1	20041230	US 2004-812702	20040330

PRIORITY APPLN. INFO.:

US 1999-115125P	P	19990106
US 2000-477148	B1	20000104
US 2002-268730	A2	20021009
US 2003-601518	A2	20030620
US 2004-802875	A2	20040312
US 2004-812702	A	20040330

AB The present invention is directed to detection and measurement of gene transcripts and their equivalent nucleic acid products in blood. Specifically provided is anal. performed on a drop of blood for detecting, diagnosing, and monitoring diseases, and in particular mental depression, using gene-specific and/or tissue-specific primers. Affymetrix Human Genome U133 and ChondroChip microarrays were used to detect differentially **expressed** gene transcripts in hypertension, obesity, allergy, systemic steroids, coronary artery disease, diabetes type 2, hyperlipidemia, lung disease, bladder cancer, rheumatoid arthritis, osteoarthritis, liver cancer, schizophrenia, Chagas disease, asthma, and manic depression syndrome. The present invention describes methods by which delineation of the sequence and/or quantitation of the **expression** levels of disease-specific genes allows for an immediate and accurate diagnostic/prognostic test for disease or to assess the effect of a particular treatment regimen. [This abstract record is one of 3 records for this document necessitated by the large number of index entries required to fully index the document and publication system constraints.].

L14 ANSWER 8 OF 21 HCAPLUS COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER: 2005:139370 HCAPLUS
DOCUMENT NUMBER: 142:195819
TITLE: Gene **expression** profiles and biomarkers for the detection of Chagas disease and other disease-related gene transcripts in blood
INVENTOR(S): Liew, Choong-Chin
PATENT ASSIGNEE(S): Chondrogene Limited, Can.
SOURCE: U.S. Pat. Appl. Publ., 154 pp., Cont.-in-part of U.S. Ser. No. 802,875.
CODEN: USXXCO
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 46
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
US 2004241729	A1	20041202	US 2004-813097	20040330
US 2004014059	A1	20040122	US 2002-268730	20021009
US 2004241729	A1	20041202	US 2004-813097	20040330

PRIORITY APPLN. INFO.:

US 1999-115125P	P	19990106
US 2000-477148	B1	20000104
US 2002-268730	A2	20021009
US 2003-601518	A2	20030620
US 2004-802875	A2	20040312
US 2004-813097	A	20040330

AB The present invention is directed to detection and measurement of gene

transcripts and their equivalent nucleic acid products in blood. Specifically
provided is anal. performed on a drop of blood for detecting, diagnosing, and monitoring diseases, and in particular Chagas disease, using gene-specific and/or tissue-specific primers. Affymetrix Human Genome U133 and ChondroChip microarrays were used to detect differentially **expressed** gene transcripts in hypertension, obesity, allergy, systemic steroids, coronary artery disease, diabetes type 2, hyperlipidemia, lung disease, bladder cancer, rheumatoid arthritis, osteoarthritis, liver cancer, schizophrenia, Chagas disease, asthma, and manic depression syndrome. The present invention describes methods by which delineation of the sequence and/or quantitation of the **expression** levels of disease-specific genes allows for an immediate and accurate diagnostic/prognostic test for disease or to assess the effect of a particular treatment regimen. [This abstract record is one of 3 records for this document necessitated by the large number of index entries required to fully index the document and publication system constraints.].

L14 ANSWER 9 OF 21 HCAPLUS COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER: 2005:112848 HCAPLUS
DOCUMENT NUMBER: 142:153468
TITLE: Gene **expression** profiles and biomarkers for the detection of lung disease-related and other disease-related gene transcripts in blood
INVENTOR(S): Liew, Choong-chin
PATENT ASSIGNEE(S): Chondrogene Limited, Can.
SOURCE: U.S. Pat. Appl. Publ., 155 pp., Cont.-in-part of U.S. Ser. No. 802,875.
CODEN: USXXCO
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 46
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.		DATE
US 2004241728	A1	20041202	US 2004-812764		20040330
US 2004014059	A1	20040122	US 2002-268730		20021009
US 2004241728	A1	20041202	US 2004-812764		20040330
PRIORITY APPLN. INFO.:			US 1999-115125P	P	19990106
			US 2000-477148	B1	20000104
			US 2002-268730	A2	20021009
			US 2003-601518	A2	20030620
			US 2004-802875	A2	20040312
			US 2004-812764	A	20040330

AB The present invention is directed to detection and measurement of gene transcripts and their equivalent nucleic acid products in blood. Specifically
provided is anal. performed on a drop of blood for detecting, diagnosing and monitoring diseases using gene-specific and/or tissue-specific primers. Affymetrix Human Genome U133 and ChondroChip microarrays were used to detect differentially **expressed** gene transcripts in hypertension, obesity, allergy, systemic steroids, coronary artery disease, diabetes type 2, hyperlipidemia, lung disease, bladder cancer, rheumatoid arthritis, osteoarthritis, liver cancer, schizophrenia, Chagas disease, asthma, and manic depression syndrome. The present invention also describes methods by which delineation of the sequence and/or quantitation of the **expression** levels of disease-specific genes allows for an immediate and accurate diagnostic/prognostic test for disease or to assess the effect of a particular treatment regimen. [This abstract record is one of 3 records for this document necessitated by the large number of index entries required to fully index the document and

publication system constraints.].

L14 ANSWER 10 OF 21 HCAPLUS COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER: 2005:248643 HCAPLUS
DOCUMENT NUMBER: 142:274056
TITLE: Sequences of human schizophrenia related genes and use for diagnosis, prognosis and therapy
INVENTOR(S): Liew, Choong-Chin
PATENT ASSIGNEE(S): Chondrogene Limited, Can.
SOURCE: U.S. Pat. Appl. Publ., 156 pp., Cont.-in-part of U.S. Ser. No. 802,875.
CODEN: USXXCO
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 46
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
US 2004241727	A1	20041202	US 2004-812731	20040330
US 2004014059	A1	20040122	US 2002-268730	20021009
US 2004241727	A1	20041202	US 2004-812731	20040330

PRIORITY APPLN. INFO.:

US 1999-115125P	P	19990106
US 2000-477148	B1	20000104
US 2002-268730	A2	20021009
US 2003-601518	A2	20030620
US 2004-802875	A2	20040312
US 2004-812731	A	20040330

AB The present invention is directed to detection and measurement of gene transcripts and their equivalent nucleic acid products in blood. Specifically provided is anal. performed on a drop of blood for detecting, diagnosing and monitoring diseases using gene-specific and/or tissue-specific primers. The present invention also describes methods by which delineation of the sequence and/or quantitation of the **expression** levels of disease-specific genes allows for an immediate and accurate diagnostic/prognostic test for disease or to assess the effect of a particular treatment regimen. [This abstract record is one of 3 records for this document necessitated by the large number of index entries required to fully index the document and publication system constraints.].

L14 ANSWER 11 OF 21 HCAPLUS COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER: 2005:139367 HCAPLUS
DOCUMENT NUMBER: 142:175391
TITLE: Analysis of genetic information contained in peripheral blood for diagnosis, prognosis and monitoring treatment of allergy, infection and genetic disease in human
INVENTOR(S): Liew, Choong-Chin
PATENT ASSIGNEE(S): Chondrogene Limited, Can.
SOURCE: U.S. Pat. Appl. Publ., 155 pp., Cont.-in-part of U.S. Ser. No. 802,875.
CODEN: USXXCO
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 46
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
US 2004241726	A1	20041202	US 2004-812707	20040330
US 2004014059	A1	20040122	US 2002-268730	20021009
US 2004241726	A1	20041202	US 2004-812707	20040330

PRIORITY APPLN. INFO.: US 1999-115125P P 19990106
US 2000-477148 B1 20000104
US 2002-268730 A2 20021009
US 2003-601518 A2 20030620
US 2004-802875 A2 20040312
US 2004-812707 A 20040330

AB The present invention is directed to detection and measurement of gene transcripts and their equivalent nucleic acid products in blood. Specifically provided is anal. performed on a drop of blood for detecting, diagnosing, and monitoring diseases, and in particular allergy, using gene-specific and/or tissue-specific primers. Affymetrix Human Genome U133 and ChondroChip microarrays were used to detect differentially **expressed** gene transcripts in hypertension, obesity, allergy, systemic steroids, coronary artery disease, diabetes type 2, hyperlipidemia, lung disease, bladder cancer, rheumatoid arthritis, osteoarthritis, liver cancer, schizophrenia, Chagas disease, asthma, and manic depression syndrome. The present invention describes methods by which delineation of the sequence and/or quantitation of the **expression** levels of disease-specific genes allows for an immediate and accurate diagnostic/prognostic test for disease or to assess the effect of a particular treatment regimen. [This abstract record is one of 3 records for this document necessitated by the large number of index entries required to fully index the document and publication system constraints.].

L14 ANSWER 12 OF 21 MEDLINE on STN DUPLICATE 4
ACCESSION NUMBER: 2003297409 MEDLINE
DOCUMENT NUMBER: PubMed ID: 12824502
TITLE: Structural analysis of UBL5, a novel ubiquitin-like modifier.
AUTHOR: McNally Teresa; Huang Qiulong; Janis Richard S; Liu Zhihong; Olejniczak Edward T; Reilly Regina M
CORPORATE SOURCE: Global Pharmaceutical Research and Discovery, Abbott Laboratories, 100 Abbott Park Road, Abbott Park, IL 60064-6100, USA.
SOURCE: Protein science : a publication of the Protein Society, (2003 Jul) 12 (7) 1562-6.
Journal code: 9211750. ISSN: 0961-8368.
PUB. COUNTRY: United States
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 200411
ENTRY DATE: Entered STN: 20030626
Last Updated on STN: 20031218
Entered Medline: 20041102

AB UBL5 is a widely **expressed** human protein that is strongly conserved across phylogeny. Orthologs of UBL5 occur in every eukaryotic genome characterized to date. The yeast ortholog of UBL5, HUB1, was reported to be a ubiquitin-like protein modifier important for modulation of protein function. However, unlike ubiquitin and all other ubiquitin-like modifiers, UBL5 and its yeast ortholog HUB1 both contain a C-terminal di-tyrosine motif followed by a single variable residue instead of the characteristic di-glycine found in all other ubiquitin-like modifiers. Here we describe the three-dimensional structure of UBL5 determined by NMR. The overall structure of the protein was found to be very similar to ubiquitin despite the low approximately 25% residue similarity. The signature C-terminal di-tyrosine residues in UBL5 are involved in the final beta sheet of the protein. This is very different to the di-glycine motif found in ubiquitin, which extends beyond the final beta sheet. In addition, we have confirmed an earlier report of an interaction between UBL5 and the cyclin-like kinase, **CLK4**, which

we have determined is specific and does not extend to other cyclin-like kinase family members.

L14 ANSWER 13 OF 21 MEDLINE on STN DUPLICATE 5
ACCESSION NUMBER: 2003187456 MEDLINE
DOCUMENT NUMBER: PubMed ID: 12705895
TITLE: Beacon interacts with cdc2/cdc28-like kinases.
AUTHOR: Kantham Lakshmi; Kerr-Bayles Lyndal; Godde Nathan; Quick Melissa; Webb Ryan; Sunderland Terry; Bond Judy; Walder Ken; Augert Guy; Collier Greg
CORPORATE SOURCE: Metabolic Research Unit, School of Health Sciences, Deakin University, Waurn Ponds 3217, Vic., Australia. kantham@deakin.edu.au. <kantham@deakin.edu.au>
SOURCE: Biochemical and biophysical research communications, (2003 Apr 25) 304 (1) 125-9.
Journal code: 0372516. ISSN: 0006-291X.
PUB. COUNTRY: United States
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 200305
ENTRY DATE: Entered STN: 20030423
Last Updated on STN: 20030521
Entered Medline: 20030520

AB Previously we found elevated beacon gene **expression** in the hypothalamus of obese Psammomys obesus. Beacon administration into the lateral ventricle of P. obesus stimulated food intake and body weight gain. In the current study we used yeast two-hybrid technology to screen for proteins in the human brain that interact with beacon. **CLK4** , an isoform of cdc2/cdc28-like kinase family of proteins, was identified as a strong interacting partner for beacon. Using active **recombinant** proteins and a surface plasmon resonance based detection technique, we demonstrated that the three members of this subfamily of kinases (CLK1, 2, and 4) all interact with beacon. Based on the known sequence and functional properties of beacon and CLKs, we speculate that beacon could either modulate the function of key regulatory molecules such as PTP1B or control the **expression** patterns of specific genes involved in the central regulation of energy metabolism.

L14 ANSWER 14 OF 21 HCAPLUS COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER: 2002:634503 HCAPLUS
DOCUMENT NUMBER: 137:227709
TITLE: Leukocyte gene **expression** profiling and diagnostic oligonucleotide probe arrays for diagnosis of leukocyte-related diseases
INVENTOR(S): Wohlgemuth, Jay; Fry, Kirk; Matcuk, George; Altman, Peter; Prentice, James; Phillips, Julie; Ly, Ngoc; Woodward, Robert; Quertermous, Thomas; Johnson, Frances
PATENT ASSIGNEE(S): Biocardia, Inc., USA
SOURCE: PCT Int. Appl., 2038 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 9
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2002057414	A2	20020725	WO 2001-XB47856	20011022

W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR,

LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PH, PL,
PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG,
US, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY,
DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF,
BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG

WO 2002057414 A2 20020725 WO 2001-US47856 20011022
WO 2002057414 A3 20020926
WO 2002057414 C2 20030912
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN,
CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH,
GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR,
LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PH, PL,
PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG,
US, UZ, VN, YU, ZA, ZW
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW, AM, AZ, BY, KG,
KZ, MD, RU, TJ, TM, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR,
IE, IT, LU, MC, NL, PT, SE, TR, BF, BJ, CF, CG, CI, CM, GA, GN,
GQ, GW, ML, MR, NE, SN, TD, TG

ZA 2003003132 A 20040923 ZA 2003-3132 20011022
PRIORITY APPLN. INFO.: US 2000-241994P P 20001020
US 2001-296764P P 20010608
WO 2001-US47856 W 20011022

AB Leukocyte gene **expression** profiling is utilized to identify oligonucleotides from gene **expression** candidate libraries. Thus, 8143 members of a candidate nucleotide library that are differentially **expressed** in activated leukocytes and resting leukocytes are provided. Oligonucleotide probes for members of the **expression** libraries are generally immobilized on an array. Diagnostic oligonucleotide sets for anal. of leukocyte-related diseases are described. [This abstract record is one of two records for this document necessitated by the large number of index entries required to fully index the document and publication system constraints.].

L14 ANSWER 15 OF 21 MEDLINE on STN DUPLICATE 6
ACCESSION NUMBER: 2002666110 MEDLINE
DOCUMENT NUMBER: PubMed ID: 12169693
TITLE: Novel SR-rich-related protein clasp specifically interacts with inactivated **Clk4** and induces the exon EB inclusion of Clk.
AUTHOR: Katsu Rieko; Onogi Hiroshi; Wada Kazuhiro; Kawaguchi Yasushi; Hagiwara Masatoshi
CORPORATE SOURCE: Department of Functional Genomics, Medical Research Institute, Tokyo Medical and Dental University, 1-5-45 Yushima, Bunkyo-ku, Japan.
SOURCE: Journal of biological chemistry, (2002 Nov 15) 277 (46) 44220-8. Electronic Publication: 2002-08-06. Journal code: 2985121R. ISSN: 0021-9258.
PUB. COUNTRY: United States
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
OTHER SOURCE: GENBANK-AB080582; GENBANK-AB080583
ENTRY MONTH: 200301
ENTRY DATE: Entered STN: 20021113
Last Updated on STN: 20030103
Entered Medline: 20030102

AB We identified a novel serine/arginine (SR)-rich-related protein as a binding partner of **Clk4** mutant lacking kinase activity (**Clk4** K189R) in the two-hybrid screen and designated it Clasp (**Clk4**-associating SR-related protein). Northern blot analysis revealed that Clasp mRNA was highly **expressed** in brain, and in situ hybridization of a mouse brain sagittal section hybridized with

antisense probes revealed that both Clasp and **Clk4** mRNAs were **expressed** in the hippocampus, the cerebellum, and the olfactory bulb. Two forms of Clasp were produced by a frameshift following alternative splicing. The staining of an HA-tagged short form of Clasp (ClaspS) showed a nucleoplasmic pattern, while the long form of Clasp (ClaspL) was localized as nuclear dots. In vitro protein interaction assay demonstrated that **Clk4** K189R was bound to Clasp while wild **Clk4** was not. Overexpression of ClaspL promoted accumulation of **Clk4** K189R in the nuclear dots and the exon EB inclusion from CR-1 and CR-2 pre-mRNA of Clk1. These data suggest that Clasp is a binding partner of **Clk4** and may be involved in the regulation of the activity of Clk kinase family.

L14 ANSWER 16 OF 21 HCAPLUS COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER: 2001:319943 HCAPLUS
DOCUMENT NUMBER: 134:336712
TITLE: Protein and cDNA sequences of a novel human cell cycle-regulating protein 53 and diagnostic and therapeutic uses thereof
INVENTOR(S): Mao, Yumin; Xie, Yi
PATENT ASSIGNEE(S): Shanghai Bio Road Gene Development Ltd., Peop. Rep. China
SOURCE: PCT Int. Appl., 30 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: Chinese
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2001030833	A1	20010503	WO 2000-CN328	20001016

W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CR, CU, CZ, DE, DK, DM, DZ, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG

PRIORITY APPLN. INFO.: CN 1999-119816 A 19991022
AB The invention provides protein and cDNA sequences for a novel human cell cycle-regulating protein 53, which is a novel member of SR protein kinase family. The human cell cycle-regulating protein 53 gene shares sequence homol. with mouse gene **CLK4**. The invention also relates to constructs and methods to **express** the **cloned** gene for the preparation of its protein and antibodies using E.coli cells or eukaryotic cells, and diagnostic and therapeutic uses for cell cycle-regulating protein 53 related diseases.
REFERENCE COUNT: 4 THERE ARE 4 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L14 ANSWER 17 OF 21 HCAPLUS COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER: 2001:507091 HCAPLUS
DOCUMENT NUMBER: 136:178643
TITLE: A set of 840 mouse oocyte genes with well-matched human homologs
AUTHOR(S): Stanton, J. L.; Green, D. P. L.
CORPORATE SOURCE: Department of Anatomy and Structural Biology, Medical School, University of Otago, Dunedin, N. Z.
SOURCE: Molecular Human Reproduction (2001), 7(6), 521-543

CODEN: MHREFD; ISSN: 1360-9947
PUBLISHER: Oxford University Press
DOCUMENT TYPE: Journal
LANGUAGE: English
AB GenBank contains 14,477 **expressed** sequence tags (EST) derived from mouse oocyte cDNA libraries: 3499 of these are from two unfertilized oocyte libraries and 10,978 are from two fertilized oocyte libraries. Gene **expression** profiles were obtained for these libraries by matching library EST to UniGene clusters. The 14,477 EST identified 4226 UniGenes. These were screened using HomoloGene to identify 1386 homologous UniGene clusters in two other species with one of the matches being human. Within these human matches, 840 encoded named proteins, 223 encoded hypothetical proteins, and 323 encoded clustered EST. The set of named genes provides the first step in establishing a database of genes **expressed** in mouse oocytes and, by extension, human oocytes.
REFERENCE COUNT: 27 THERE ARE 27 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L14 ANSWER 18 OF 21 MEDLINE on STN DUPLICATE 7
ACCESSION NUMBER: 2001393555 MEDLINE
DOCUMENT NUMBER: PubMed ID: 11170754
TITLE: Molecular characterization of a cDNA encoding functional human **CLK4** kinase and localization to chromosome 5q35 [correction of 4q35].
COMMENT: Erratum in: Genomics 2001 Jun 1;74(2):251
AUTHOR: Schultz J; Jones T; Bork P; Sheer D; Blencke S; Steyrer S; Wellbrock U; Bevec D; Ullrich A; Wallasch C
CORPORATE SOURCE: Axxima Pharmaceuticals AG, Am Klopferspitz 19, Martinsried, D-82152, Germany.
SOURCE: Genomics, (2001 Feb 1) 71 (3) 368-70.
Journal code: 8800135. ISSN: 0888-7543.
PUB. COUNTRY: United States
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
OTHER SOURCE: GENBANK-AA449725; GENBANK-AA631990; GENBANK-AF294429; GENBANK-AI004959; GENBANK-AI039778; GENBANK-AI094075; GENBANK-H29221
ENTRY MONTH: 200107
ENTRY DATE: Entered STN: 20010716
Last Updated on STN: 20020420
Entered Medline: 20010712
AB Phosphorylated serine- and arginine-rich (SR) proteins play an important role in the formation of spliceosomes, possibly controlling the regulation of alternative splicing. Enzymes that phosphorylate the SR proteins belong to the family of CDC2/CDC28-like kinases (CLK). Employing nucleotide sequence comparison of human **expressed** sequence tag sequences to the murine counterpart, we identified, **cloned**, and recombinantly **expressed** the human orthologue to the murine **CLK4** cDNA. When fused to glutathione S-transferase, the catalytically active human **CLK4** is able to autophosphorylate and to phosphorylate myelin basic protein, but not histone H2B as a substrate. Inspection of mRNA accumulation demonstrated gene **expression** in all human tissues, with the most prominent abundance in liver, kidney, brain, and heart. Using fluorescence in situ hybridization, the human **CLK4** cDNA was localized to band q35 on chromosome 5 [corrected].
Copyright 2001 Academic Press.

L14 ANSWER 19 OF 21 HCAPLUS COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER: 2001:394028 HCAPLUS
DOCUMENT NUMBER: 138:101609
TITLE: Molecular characterization of a cDNA encoding functional human **CLK4** kinase and

localization to chromosome 5q35. [Erratum to document cited in CA135:206183]
AUTHOR(S): Schultz, Jorg; Jones, Tania; Bork, Peer; Sheer, Denise; Blencke, Stephanie; Steyrer, Silvia; Wellbrock, Ursula; Bevec, Dorian; Ullrich, Axel; Wallasch, Christian
CORPORATE SOURCE: EMBL, Heidelberg, D-69012, Germany
SOURCE: Genomics (2001), 74(2), 251
CODEN: GNMCEP; ISSN: 0888-7543
PUBLISHER: Academic Press
DOCUMENT TYPE: Journal
LANGUAGE: English
AB The **CLK4** gene should have been assigned to chromosome band 5q35 instead of to 4q35. On pages 368 and 369, in the title, abstract, and Figure 2, all refs. to the chromosomal mapping should be changed to read chromosome 5 band q35 (or 5q35, when appropriate). The corrected Figure 2 with its legend is given. (c) 2001 Academic Press.

L14 ANSWER 20 OF 21 HCAPLUS COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER: 1997:646068 HCAPLUS
DOCUMENT NUMBER: 127:343285
TITLE: Characterization and comparison of four serine- and arginine-rich (SR) protein kinases
AUTHOR(S): Nayler, Oliver; Stamm, Stefan; Ullrich, Axel
CORPORATE SOURCE: Max-Planck-Institute for Biochemistry, Martinsried, D-82152, Germany
SOURCE: Biochemical Journal (1997), 326(3), 693-700
CODEN: BIJOAK; ISSN: 0264-6021
PUBLISHER: Portland Press
DOCUMENT TYPE: Journal
LANGUAGE: English
AB Phosphorylated serine- and arginine-rich (SR) proteins are components of the spliceosomal complex, and have been implicated in the control of alternative splicing. Kinases that regulate the phosphorylation and possibly the intranuclear distribution of SR proteins may therefore contribute to changes in choice of splice site. We have **cloned** three mouse cDNAs with high sequence identity to the family of LAMMER kinases (i.e. kinases carrying the conserved signature EHLAMMERILG in the catalytic domain). A comparison of their amino acid sequences revealed two related subfamilies with high evolutionary conservation. We have compared the **expression** patterns of these proteins in mouse tissues and transformed cell lines with that of a previously **cloned** family member (mCLK1/STY), and detected various transcripts for each gene. This underlines previous findings of alternative splicing of mclk1/STY. Our results suggest that the proportions of products for each gene are regulated independently. We further demonstrate that all variants encode autophosphorylating proteins that can phosphorylate several biochem. purified SR proteins in vitro, leading to hyperphosphorylation of at least one SR protein in vivo. The observed tissue distributions and substrate specificities suggest that these kinases may all be constituents of a network of regulatory mechanisms that enable SR proteins to control RNA splicing.
REFERENCE COUNT: 33 THERE ARE 33 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L14 ANSWER 21 OF 21 MEDLINE on STN DUPLICATE 8
ACCESSION NUMBER: 97480726 MEDLINE
DOCUMENT NUMBER: PubMed ID: 9339371
TITLE: Construction of a 3-Mb contig and partial transcript map of the central region of mouse chromosome 11.
AUTHOR: Watkins-Chow D E; Douglas K R; Buckwalter M S; Probst F J;

Camper S A
CORPORATE SOURCE: Department of Human Genetics, University of Michigan Medical School, Ann Arbor 48109, USA.
CONTRACT NUMBER: HD30428 (NICHD)
P30HG00209 (NHGRI)
T32GM07863 (NIGMS)
+
SOURCE: Genomics, (1997 Oct 1) 45 (1) 147-57.
Journal code: 8800135. ISSN: 0888-7543.
PUB. COUNTRY: United States
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
OTHER SOURCE: GENBANK-G31366; GENBANK-G31367; GENBANK-G31368; GENBANK-G31369; GENBANK-G31370; GENBANK-G31371; GENBANK-G31372; GENBANK-G31373; GENBANK-G31414; GENBANK-G31415; GENBANK-G31416; GENBANK-G31417; GENBANK-G31418; GENBANK-G31419; GENBANK-G31420; GENBANK-G31421; GENBANK-G31422; GENBANK-G31423; GENBANK-G31424; GENBANK-G31425; GENBANK-G31426; GENBANK-G31427; GENBANK-G31428; GENBANK-G31429; GENBANK-G31430; GENBANK-G31431; GENBANK-G31432; GENBANK-G31433
ENTRY MONTH: 199711
ENTRY DATE: Entered STN: 19971224
Last Updated on STN: 19990129
Entered Medline: 19971120

AB We report the establishment of a high-resolution genetic map, a physical map, and a partial transcript map of the Ames dwarf critical region on mouse chromosome 11. A contig of 24 YACs and 13 P1 **clones** has been assembled and spans approximately 3 Mb from Flt4 to Tcf7. A library of approximately 1000 putative transcript **clones** from the region was prepared using exon amplification and pituitary cDNA selection. Ten novel transcripts were partially characterized, including a member of the olfactory receptor family, an alpha-tubulin-related sequence, and a novel member of the cdc2/CDC28-like kinase family, **Clk4**. The location of Prop1, the gene responsible for Ames dwarfism, has been localized within the contig. This contig spans a region of mouse chromosome 11 that exhibits linkage conservation with human chromosome 5q23-q35. The strength of the genetic map and genomic resources for this region suggest that comparative DNA sequencing of this region could reveal the genes responsible for other mouse mutants and human genetic diseases.

=> d his

(FILE 'HOME' ENTERED AT 12:23:37 ON 28 JUL 2005)

FILE 'MEDLINE, EMBASE, BIOSIS, BIOTECHDS, SCISEARCH, HCAPLUS, NTIS, LIFESCI' ENTERED AT 12:24:27 ON 28 JUL 2005

L1 1340563 S KINASE?
L2 441287 S SERINE OR THREONINE
L3 111458 S L1 AND L2
L4 30908 S "CDC"
L5 285 S L3 AND L4
L6 7187685 S CLON? OR EXPRESS? OR RECOMBINANT
L7 142 S L5 AND L6
L8 112 DUP REM L7 (30 DUPLICATES REMOVED)
L9 63 S HUMAN AND L8
L10 126 S "SERINE AND ARGININE RICH"
L11 1 S L9 AND L10
L12 58 S "CLK4"
L13 48 S L6 AND L12

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L14          21 DUP REM L13 (27 DUPLICATES REMOVED)

=> e yan c/au
E1            1     YAN BUYU/AU
E2            1     YAN BY ZHANQING/AU
E3         1170 --> YAN C/AU
E4            3     YAN C B/AU
E5          128     YAN C C/AU
E6           11     YAN C C S/AU
E7            3     YAN C CHAN/AU
E8           19     YAN C D/AU
E9           29     YAN C F/AU
E10          58     YAN C G/AU
E11         510     YAN C H/AU
E12           3     YAN C H F/AU

=> s e3
L15        1170 "YAN C"/AU

=> e ye j/au
E1            2     YE IN HAE/AU
E2            1     YE INN SUK/AU
E3         1942 --> YE J/AU
E4            1     YE JRX/AU
E5           17     YE J A/AU
E6          243     YE J B/AU
E7           42     YE J C/AU
E8           44     YE J D/AU
E9           23     YE J F/AU
E10          14     YE J G/AU
E11         402     YE J H/AU
E12         142     YE J J/AU

=> s e3
L16        1942 "YE J"/AU

=> e ketchum k a/au
E1            1     KETCHUM JR R L/AU
E2           34     KETCHUM K/AU
E3          236 --> KETCHUM K A/AU
E4            1     KETCHUM K J/AU
E5           34     KETCHUM K L/AU
E6           23     KETCHUM KAREN/AU
E7          188     KETCHUM KAREN A/AU
E8            1     KETCHUM KAREN ANN/AU
E9            2     KETCHUM KATHY/AU
E10           2     KETCHUM KATHY L/AU
E11           4     KETCHUM KEVIN/AU
E12           3     KETCHUM KEVIN L/AU

=> s e3-e7
L17         482 ("KETCHUM K A"/AU OR "KETCHUM K J"/AU OR "KETCHUM K L"/AU OR
                "KETCHUM KAREN"/AU OR "KETCHUM KAREN A"/AU)

=> e beasley e m/au
E1            1     BEASLEY E H/AU
E2            6     BEASLEY E L/AU
E3          330 --> BEASLEY E M/AU
E4            7     BEASLEY E O/AU
E5            1     BEASLEY E S G/AU
E6            2     BEASLEY E T/AU
E7            4     BEASLEY E W/AU
E8            2     BEASLEY E W 3RD/AU
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E9            2     BEASLEY E W III/AU
E10           1     BEASLEY E W JR/AU
E11           1     BEASLEY EDWARD E/AU
E12           1     BEASLEY EDWARD EVANS/AU

=> s e3
L18         330 "BEASLEY E M"/AU

=> e difrancesco v/au
E1            1     DIFRANCESCO U/AU
E2            1     DIFRANCESCO U M/AU
E3           80 --> DIFRANCESCO V/AU
E4           17     DIFRANCESCO VALENTINA/AU
E5            1     DIFRANCESCOL/AU
E6            1     DIFRANCESO D/AU
E7            2     DIFRANCESO L/AU
E8            1     DIFRANCESO R/AU
E9            1     DIFRANCESO ROBIN/AU
E10           6     DIFRANCIA C/AU
E11           4     DIFRANCIA CELENE/AU
E12          13     DIFRANCIA G/AU

=> s e3-e4
L19          97 ("DIFRANCESCO V"/AU OR "DIFRANCESCO VALENTINA"/AU)

=> d his

     (FILE 'HOME' ENTERED AT 12:23:37 ON 28 JUL 2005)

     FILE 'MEDLINE, EMBASE, BIOSIS, BIOTECHDS, SCISEARCH, HCAPLUS, NTIS,
     LIFESCI' ENTERED AT 12:24:27 ON 28 JUL 2005
L1       1340563 S KINASE?
L2        441287 S SERINE OR THREONINE
L3        111458 S L1 AND L2
L4         30908 S "CDC"
L5           285 S L3 AND L4
L6       7187685 S CLON? OR EXPRESS? OR RECOMBINANT
L7           142 S L5 AND L6
L8           112 DUP REM L7 (30 DUPLICATES REMOVED)
L9            63 S HUMAN AND L8
L10          126 S "SERINE AND ARGININE RICH"
L11            1 S L9 AND L10
L12           58 S "CLK4"
L13           48 S L6 AND L12
L14           21 DUP REM L13 (27 DUPLICATES REMOVED)
                 E YAN C/AU
L15         1170 S E3
                 E YE J/AU
L16         1942 S E3
                 E KETCHUM K A/AU
L17          482 S E3-E7
                 E BEASLEY E M/AU
L18          330 S E3
                 E DIFRANCESCO V/AU
L19           97 S E3-E4

=> s l15 or l16 or l17 or l18 or l19
L20         3708 L15 OR L16 OR L17 OR L18 OR L19

=> s l20 and l5
L21            0 L20 AND L5

=> s l2 and l20
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<------User Break------>

SEARCH ENDED BY USER

=> s l12 and l20
L22 0 L12 AND L20

=> s l4 and l20
L23 1 L4 AND L20

=> d all

L23 ANSWER 1 OF 1 MEDLINE on STN
AN 2004260824 IN-PROCESS
DN PubMed ID: 15160106
TI Study on inspection method of anaerobes in periodontal pockets.
AU Li D Y; Zhang G C; **Ye J**
CS Shanghai Second Medical University, Shanghai Research Institute of Stomatology. Shanghai 200011,China.
SO Shanghai Kou Qiang Yi Xue, (1995 Mar) 4 (1) 30-2.
Journal code: 101090220. ISSN: 1006-7248.
CY China
DT Journal; Article; (JOURNAL ARTICLE)
LA Chinese
FS NONMEDLINE; IN-DATA-REVIEW; IN-PROCESS; NONINDEXED
ED Entered STN: 20040526
Last Updated on STN: 20041219
AB This paper used two methods only use non-selective medium(**CDC**) and together with seven selective mediums(VS CS BS AS FS ES LS) to inspect anaerobes in periodontal pockets.The results showed that Gram-negative anaerobes were the predominant microflora of periodontitis.The method of **CDC** together with selective mediums was founded much simpler and faster,more valuable than the method of only use non-selective medium.It is illustrated that **CDC** added antibiotics or chemicals to make selective mediums was prepared convenience and was suitable for growth of relative anaerobes.But it is still necessary to establish much more,more special, more reliable selective or identical mediums.

=> d his

(FILE 'HOME' ENTERED AT 12:23:37 ON 28 JUL 2005)

FILE 'MEDLINE, EMBASE, BIOSIS, BIOTECHDS, SCISEARCH, HCAPLUS, NTIS, LIFESCI' ENTERED AT 12:24:27 ON 28 JUL 2005

L1 1340563 S KINASE?
L2 441287 S SERINE OR THREONINE
L3 111458 S L1 AND L2
L4 30908 S "CDC"
L5 285 S L3 AND L4
L6 7187685 S CLON? OR EXPRESS? OR RECOMBINANT
L7 142 S L5 AND L6
L8 112 DUP REM L7 (30 DUPLICATES REMOVED)
L9 63 S HUMAN AND L8
L10 126 S "SERINE AND ARGININE RICH"
L11 1 S L9 AND L10
L12 58 S "CLK4"
L13 48 S L6 AND L12
L14 21 DUP REM L13 (27 DUPLICATES REMOVED)
E YAN C/AU
L15 1170 S E3
E YE J/AU
L16 1942 S E3

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                E KETCHUM K A/AU
L17          482 S E3-E7
                E BEASLEY E M/AU
L18          330 S E3
                E DIFRANCESCO V/AU
L19           97 S E3-E4
L20         3708 S L15 OR L16 OR L17 OR L18 OR L19
L21            0 S L20 AND L5
L22            0 S L12 AND L20
L23            1 S L4 AND L20

=> s l10 and l20
L24            0 L10 AND L20

=> d his

     (FILE 'HOME' ENTERED AT 12:23:37 ON 28 JUL 2005)

     FILE 'MEDLINE, EMBASE, BIOSIS, BIOTECHDS, SCISEARCH, HCAPLUS, NTIS,
     LIFESCI' ENTERED AT 12:24:27 ON 28 JUL 2005
L1       1340563 S KINASE?
L2        441287 S SERINE OR THREONINE
L3        111458 S L1 AND L2
L4         30908 S "CDC"
L5           285 S L3 AND L4
L6       7187685 S CLON? OR EXPRESS? OR RECOMBINANT
L7           142 S L5 AND L6
L8           112 DUP REM L7 (30 DUPLICATES REMOVED)
L9            63 S HUMAN AND L8
L10          126 S "SERINE AND ARGININE RICH"
L11            1 S L9 AND L10
L12           58 S "CLK4"
L13           48 S L6 AND L12
L14           21 DUP REM L13 (27 DUPLICATES REMOVED)
                E YAN C/AU
L15         1170 S E3
                E YE J/AU
L16         1942 S E3
                E KETCHUM K A/AU
L17          482 S E3-E7
                E BEASLEY E M/AU
L18          330 S E3
                E DIFRANCESCO V/AU
L19           97 S E3-E4
L20         3708 S L15 OR L16 OR L17 OR L18 OR L19
L21            0 S L20 AND L5
L22            0 S L12 AND L20
L23            1 S L4 AND L20
L24            0 S L10 AND L20
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	L #	Hits	Search Text
1	L1	61817	kinase$2
2	L2	0	"serine and arginine rich"
3	L3	753	"CDC like" or "CLK4"
4	L4	754486	clon$3 or express$3 or recombinant
5	L5	60	l3 same l4
6	L6	41	l1 and l5
7	L7	0	"cdc like kinase$2"
8	L8	55	l1 same l3
9	L9	22581	YAN YE KETCHUM BEASLEY DIFRANCESCO
10	L10	12	l8 and l9
11	L11	10	l6 and l9

	Issue Date	Pages	Document ID	Title
1	20050714	148	US 20050152908 A1	Liver cancer biomarkers
2	20050505	40	US 20050095607 A1	Breast cancer signatures
3	20050407	145	US 20050074850 A1	Novel calcium channels and uses thereof
4	20050407	107	US 20050074793 A1	Metastatic colorectal cancer signatures
5	20050317	55	US 20050059153 A1	Electromagnetic activation of gene expression and cell growth
6	20041209	31	US 20040248136 A1	Method of labeling nucleic acids
7	20041202	678	US 20040241653 A1	Methods for identifying marker genes for cancer
8	20041118	274	US 20040229367 A1	Methods for monitoring multiple gene expression
9	20040805	53	US 20040152123 A1	Isolated human kinase proteins, nucleic acid molecules encoding human kinase proteins, and uses thereof
10	20040701	130	US 20040127406 A1	Methods for in vitro expansion and transdifferentiation of human pancreatic acinar cells into insulin-producing cells
11	20040527	35	US 20040101915 A1	Diagnosis and treatment of chemoresistant tumors
12	20040422	253	US 20040076955 A1	Methods of diagnosis of bladder cancer, compositions and methods of screening for modulators of bladder cancer

13	20040415	275	US 20040071700 A1	Obesity linked genes

	Issue Date	Pages	Document ID	Title
14	20040325	82	US 20040058325 A1	Gene expression in biological conditions
15	20040226	621	US 20040038292 A1	Wound healing biomarkers
16	20040129	169	US 20040018527 A1	Differential patterns of gene expression that predict for docetaxel chemosensitivity and chemo resistance
17	20040122	108	US 20040014059 A1	Method for the detection of gene transcripts in blood and uses thereof
18	20040115	484	US 20040009479 A1	Methods and compositions for diagnosing or monitoring auto immune and chronic inflammatory diseases
19	20040108	345	US 20040005563 A1	Methods of diagnosis of ovarian cancer, compositions and methods of screening for modulators of ovarian cancer
20	20040101	106	US 20040002067 A1	Breast cancer progression signatures
21	20031204	29	US 20030224422 A1	Pre-and post therapy gene expression profiling to identify drug targets
22	20031127	64	US 20030219895 A1	Antisense modulation of CDC-like kinase 1 expression
23	20031127	81	US 20030219767 A1	Compositions, kits, and methods for identification, assessment, prevention, and therapy of breast cancer
24	20031106	58	US 20030207290 A1	Methods, reagents, kits and apparatus for protein function analysis

	Issue Date	Pages	Document ID	Title
25	20030717	53	US 20030134319 A1	Isolated human kinase proteins, nucleic acid molecules encoding human kinase proteins, and uses thereof
26	20030605	21	US 20030104457 A1	Method and device for detecting and monitoring alcoholism and related diseases using microarrays
27	20030508	18	US 20030087273 A1	Compositions and methods for inhibiting human immunodeficiency virus infection by down-regulating human cellular genes
28	20030501	78	US 20030082511 A1	Identification of modulatory molecules using inducible promoters
29	20030320	22	US 20030054387 A1	Metastasis-associated genes
30	20021024	753	US 20020155119 A1	Isolation and use of fetal urogenital sinus expressed sequences
31	20021003	125	US 20020142981 A1	Gene expression profiles in liver cancer
32	20020829	53	US 20020119548 A1	Isolated human kinase proteins, nucleic acid molecules encoding human kinase proteins, and uses thereof
33	20020620	52	US 20020076783 A1	Plants and plants cells expressing histidine tagged intimin
34	20020425	46	US 20020048756 A1	Analysis of gene family expression
35	20050614	470	US 6905827 B2	Methods and compositions for diagnosing or monitoring auto immune and chronic inflammatory diseases

	Issue Date	Pages	Document ID	Title
36	20050607	264	US 6902887 B1	Methods for monitoring multiple gene expression
37	20040511	50	US 6733978 B2	Isolated human kinase proteins, nucleic acid molecules encoding human kinase proteins, and uses thereof
38	20040316	434	US 6706867 B1	DNA array sequence selection
39	20031007	50	US 6630337 B2	Isolated human kinase proteins, nucleic acid molecules encoding human kinase proteins, and uses thereof
40	20020924	50	US 6455291 B1	Isolated human kinase proteins, nucleic acid molecules encoding human kinase proteins, and uses thereof
41	20010515	21	US 6232065 B1	Analysis of gene family expression

	Issue Date	Pages	Document ID	Title
1	20040805	53	US 20040152123 A1	Isolated human kinase proteins, nucleic acid molecules encoding human kinase proteins, and uses thereof
2	20040422	253	US 20040076955 A1	Methods of diagnosis of bladder cancer, compositions and methods of screening for modulators of bladder cancer
3	20040108	345	US 20040005563 A1	Methods of diagnosis of ovarian cancer, compositions and methods of screening for modulators of ovarian cancer
4	20031106	58	US 20030207290 A1	Methods, reagents, kits and apparatus for protein function analysis
5	20030717	53	US 20030134319 A1	Isolated human kinase proteins, nucleic acid molecules encoding human kinase proteins, and uses thereof
6	20020829	53	US 20020119548 A1	Isolated human kinase proteins, nucleic acid molecules encoding human kinase proteins, and uses thereof
7	20020620	52	US 20020076783 A1	Plants and plants cells expressing histidine tagged intimin
8	20040511	50	US 6733978 B2	Isolated human kinase proteins, nucleic acid molecules encoding human kinase proteins, and uses thereof
9	20031007	50	US 6630337 B2	Isolated human kinase proteins, nucleic acid molecules encoding human kinase proteins, and uses thereof

	Issue Date	Pages	Document ID	Title
10	20020924	50	US 6455291 B1	Isolated human kinase proteins, nucleic acid molecules encoding human kinase proteins, and uses thereof

	Issue Date	Pages	Document ID	Title
1	20050714	148	US 20050152908 A1	Liver cancer biomarkers
2	20050707	86	US 20050147610 A1	IL-18 binding proteins
3	20050519	57	US 20050107386 A1	Methods of treating diseases and disorders by targeting multiple kinases
4	20050512	87	US 20050100965 A1	IL-18 binding proteins
5	20050505	40	US 20050095607 A1	Breast cancer signatures
6	20050407	145	US 20050074850 A1	Novel calcium channels and uses thereof
7	20050407	107	US 20050074793 A1	Metastatic colorectal cancer signatures
8	20050317	55	US 20050059153 A1	Electromagnetic activation of gene expression and cell growth
9	20050210	10	US 20050032071 A1	RNA surveillance among curated proteins
10	20041209	31	US 20040248136 A1	Method of labeling nucleic acids
11	20041202	678	US 20040241653 A1	Methods for identifying marker genes for cancer
12	20040902	125	US 20040171823 A1	Polynucleotides and polypeptides associated with the NF-kappaB pathway
13	20040805	53	US 20040152123 A1	Isolated human kinase proteins, nucleic acid molecules encoding human kinase proteins, and uses thereof

	Issue Date	Pages	Document ID	Title
14	20040701	130	US 20040127406 A1	Methods for in vitro expansion and transdifferentiation of human pancreatic acinar cells into insulin-producing cells
15	20040617	18	US 20040115664 A1	Method of testing anticancer agent-sensitivity of tumor cells
16	20040527	35	US 20040101915 A1	Diagnosis and treatment of chemoresistant tumors
17	20040422	253	US 20040076955 A1	Methods of diagnosis of bladder cancer, compositions and methods of screening for modulators of bladder cancer
18	20040415	275	US 20040071700 A1	Obesity linked genes
19	20040325	82	US 20040058325 A1	Gene expression in biological conditions
20	20040311	152	US 20040048310 A1	Novel human protein kinases and protein kinase-like enzymes
21	20040311	46	US 20040048279 A1	Method for detecting methylation states for a toxicological diagnostic
22	20040226	621	US 20040038292 A1	Wound healing biomarkers
23	20040129	169	US 20040018527 A1	Differential patterns of gene expression that predict for docetaxel chemosensitivity and chemo resistance
24	20040122	108	US 20040014059 A1	Method for the detection of gene transcripts in blood and uses thereof

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25	20040115	484	US 20040009479 A1	Methods and compositions for diagnosing or monitoring auto immune and chronic inflammatory diseases
26	20040108	345	US 20040005563 A1	Methods of diagnosis of ovarian cancer, compositions and methods of screening for modulators of ovarian cancer
27	20040108	64	US 20040005559 A1	Markers of neuronal differentiation and morphogenesis
28	20040101	106	US 20040002067 A1	Breast cancer progression signatures
29	20031204	29	US 20030224422 A1	Pre-and post therapy gene expression profiling to identify drug targets
30	20031127	103	US 20030220224 A1	Novel polynucleotides encoding the human citron kinase polypeptide, BMSNKC_0020/0021
31	20031127	64	US 20030219895 A1	Antisense modulation of CDC-like kinase 1 expression
32	20031127	81	US 20030219767 A1	Compositions, kits, and methods for identification, assessment, prevention, and therapy of breast cancer
33	20031113	164	US 20030211476 A1	Genetic analysis of peyer's patches and M cells and methods and compositions targeting peyer's patches and M cell receptors
34	20031106	58	US 20030207290 A1	Methods, reagents, kits and apparatus for protein function analysis

	Issue Date	Pages	Document ID	Title
35	20030911	21	US 20030170673 A1	Identification of genes involved in restenosis and in atherosclerosis
36	20030814	278	US 20030154032 A1	Methods and compositions for diagnosing and treating rheumatoid arthritis
37	20030717	53	US 20030134319 A1	Isolated human kinase proteins, nucleic acid molecules encoding human kinase proteins, and uses thereof
38	20030605	21	US 20030104457 A1	Method and device for detecting and monitoring alcoholism and related diseases using microarrays
39	20030508	18	US 20030087273 A1	Compositions and methods for inhibiting human immunodeficiency virus infection by down-regulating human cellular genes
40	20030501	78	US 20030082511 A1	Identification of modulatory molecules using inducible promoters
41	20030327	41	US 20030059791 A1	Method for evaluating DNA probes position on substrate
42	20030320	22	US 20030054387 A1	Metastasis-associated genes
43	20030206	26	US 20030027230 A1	HPRP4s as modifiers of the p53 pathway and methods of use
44	20021024	753	US 20020155119 A1	Isolation and use of fetal urogenital sinus expressed sequences
45	20021003	125	US 20020142981 A1	Gene expression profiles in liver cancer
46	20020829	53	US 20020119548 A1	Isolated human kinase proteins, nucleic acid molecules encoding human kinase proteins, and uses thereof

	Issue Date	Pages	Document ID	Title
47	20020620	52	US 20020076783 A1	Plants and plants cells expressing histidine tagged intimin
48	20020425	46	US 20020048756 A1	Analysis of gene family expression
49	20020124	57	US 20020009730 A1	Human stress array
50	20050614	470	US 6905827 B2	Methods and compositions for diagnosing or monitoring auto immune and chronic inflammatory diseases
51	20040511	50	US 6733978 B2	Isolated human kinase proteins, nucleic acid molecules encoding human kinase proteins, and uses thereof
52	20040316	434	US 6706867 B1	DNA array sequence selection
53	20031007	50	US 6630337 B2	Isolated human kinase proteins, nucleic acid molecules encoding human kinase proteins, and uses thereof
54	20020924	50	US 6455291 B1	Isolated human kinase proteins, nucleic acid molecules encoding human kinase proteins, and uses thereof
55	20010515	21	US 6232065 B1	Analysis of gene family expression

	Issue Date	Pages	Document ID	Title
1	20040902	125	US 20040171823 A1	Polynucleotides and polypeptides associated with the NF-kappaB pathway
2	20040805	53	US 20040152123 A1	Isolated human kinase proteins, nucleic acid molecules encoding human kinase proteins, and uses thereof
3	20040422	253	US 20040076955 A1	Methods of diagnosis of bladder cancer, compositions and methods of screening for modulators of bladder cancer
4	20040108	345	US 20040005563 A1	Methods of diagnosis of ovarian cancer, compositions and methods of screening for modulators of ovarian cancer
5	20031127	103	US 20030220224 A1	Novel polynucleotides encoding the human citron kinase polypeptide, BMSNKC_0020/0021
6	20031106	58	US 20030207290 A1	Methods, reagents, kits and apparatus for protein function analysis
7	20030717	53	US 20030134319 A1	Isolated human kinase proteins, nucleic acid molecules encoding human kinase proteins, and uses thereof
8	20020829	53	US 20020119548 A1	Isolated human kinase proteins, nucleic acid molecules encoding human kinase proteins, and uses thereof
9	20020620	52	US 20020076783 A1	Plants and plants cells expressing histidine tagged intimin

10	20040511	50	US 6733978 B2	Isolated human kinase proteins, nucleic acid molecules encoding human kinase proteins, and uses thereof

	Issue Date	Pages	Document ID	Title
11	20031007	50	US 6630337 B2	Isolated human kinase proteins, nucleic acid molecules encoding human kinase proteins, and uses thereof
12	20020924	50	US 6455291 B1	Isolated human kinase proteins, nucleic acid molecules encoding human kinase proteins, and uses thereof